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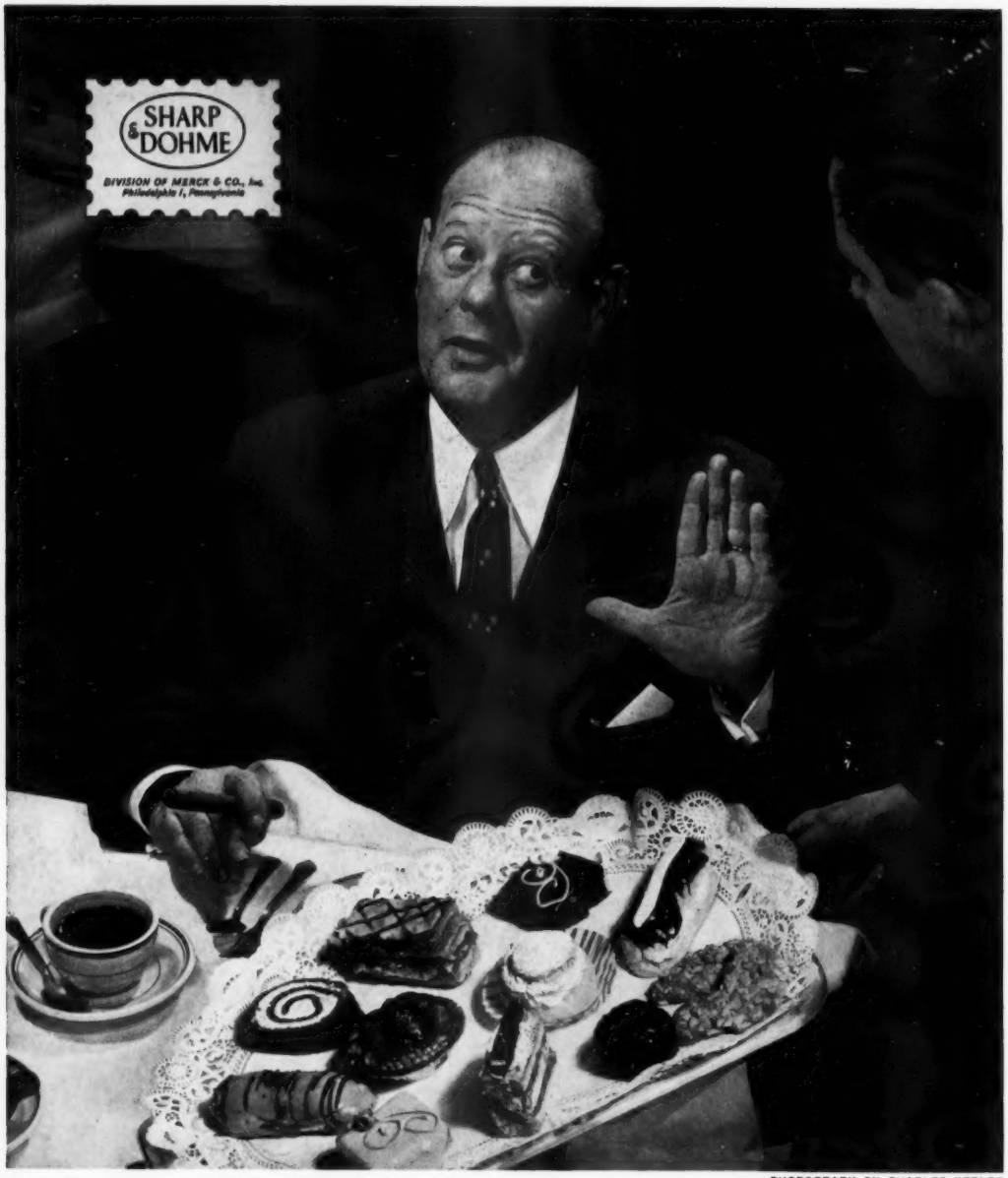

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Treatment of Cardiovascular Disease with Anticoagulants

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WRIGHT R. ADAMS

Most of the discussion about the use of anticoagulants in the treatment of thromboembolic disease has concerned whether they are worthwhile or not. I believe we no longer need to argue that point. Debate continues about just what are the indications for use and when are the undoubted benefits they confer greater than the undoubted dangers which they introduce; but I prefer to review briefly some of the indications and one or two of the principal debates, and then discuss my clinical experience with individual patients.

The use of these agents is restricted currently because adequate prothrombin time determinations are absolutely essential to their use. Such determinations do not require elaborate laboratory equipment, but they do require a very carefully trained, conscientious technician. Considerable efforts are being made to train more technicians adequately, and well-trained technicians are available in an increasing number of hospitals. I believe that before many years have passed these drugs will be used quite generally, as necessary laboratory facilities become available.

Indications for Use

We have come to use these drugs increasingly in exacerbations of coronary insufficiency. This occurs (1) when angina develops suddenly and rather severely; (2) where a pre-existing stable angina increases suddenly in severity or frequency; (3) when angina of effort suddenly becomes complicated by nocturnal angina, or status anginosus occurring with little or no effort; (4) when the progress of coronary disease indicates an acute exacerbation. It is well known that many, probably most, cases of myocardial infarction are preceded for a few days or weeks by so-called

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TABLE 1

INDICATIONS FOR ANTICOAGULANT THERAPY

1. Coronary thrombosis with myocardial infarction
2. Exacerbation of coronary insufficiency
3. Rheumatic heart disease with auricular fibrillation and emboli
4. Venous thrombosis (thrombophlebitis, phlebothrombosis, migrating thrombophlebitis)
5. Arterial embolism or thrombosis
6. Pulmonary embolism
7. Postoperatively (?)

premonitory symptoms. These symptoms are an exacerbation of the symptoms of coronary disease without an outright infarction. To the best of my knowledge no one has provided statistical proof, but certainly the use of these drugs under such circumstances seems rational. I believe these drugs will be used increasingly under such circumstances in the hope of sliding over an acute phase of the disease and allowing time for the development of collateral circulation and other adjustment to the coronary narrowing, or in the hope of actually preventing a threatening myocardial infarction.

Indications for using these drugs in rheumatic heart disease with auricular fibrillation and emboli are quite clear. I doubt that they are indicated under these circumstances unless there is actual evidence that thrombo-embolism has occurred, although some physicians contend they are desirable whenever failure and auricular fibrillation are present, particularly in older patients.

Venous thrombosis of various kinds—thrombophlebitis, phlebothrombosis, migrating thrombophlebitis—is a clear-cut indication for use, as are arterial embolism or thrombosis and pulmonary embolism from whatever cause.

I think that the postoperative use of anticoagulants to prevent thrombo-embolism is probably becoming a little less frequent. Certainly they should be used with patients who have a known tendency toward thrombo-embolic disease.

One of the principal indications for use of anticoagulant therapy, the one that has received the greatest attention, is coronary thrombosis with myocardial infarction. This subject has been much discussed and a great number of statistics are available. I have assembled a brief résumé of two sets of statistics, more to give an impression of the uncertainty and variability of the statistics at the moment than to prove anything.

Russek and his group[1] collected 1,047 cases of myocardial infarction treated without benefit of anticoagulants. He divided these patients into good risks and poor risks. A patient was put in the poor risk group if he had any one of the following: a previous myocardial infarction, intractable and long-continued pain, an extreme degree or persistence of shock, significant enlargement of the heart, gallop rhythm, heart failure, various serious arrhythmias, diabetic acidosis, obesity, previous pulmonary embolism, varicosities or thrombophlebitis. The decision to put the patient in one group or the other was made on the basis of his record and information available during his first day of hospitalization for myocardial infarction. It is not exactly clear in my mind how these investigators recognized intractable pain or long-persistent shock on the first day, but that is the stated basis of this collection of figures.

TABLE 2

MORTALITY RATE OF MILD VS. SEVERE ATTACKS OF MYOCARDIAL INFARCTION WITHOUT ANTICOAGULANT THERAPY

	NUMBER OF PATIENTS	MORTALITY RATE (*Per Cent*)
Russek et al.[1]		
"Good risk"	489	3.1
"Poor risk"	558	60.0
Total	1,047	33.4
Committee of American Heart Association[2]		
Mild to moderate	326	12.9
Severe	116	45.2
Total	442	21.5

In a group of 489 patients who were good risks—that is, patients who had had appar-

ently mild attacks or just one attack and patients who were otherwise in reasonably good health—the mortality rate was 3.1 per cent. For 558 patients who were poor risks the mortality rate was 60 per cent. The average mortality rate for the two groups combined was 33.4 per cent.

A similar array of statistics was collected from the famous American Heart Association Committee series. Several well-selected cardiologists made a controlled study of anticoagulant therapy in its early days, using some patients who were treated and some who were not. These men tried to decide on the first day of hospital admission whether the case was mild, moderate or severe. As they worked along they had a lot of difficulty in differentiating mild from moderate, and so eventually these two designations were combined.

Their results were not nearly as good as those of Russek and his group. Of a total of 442 patients, 326 were classified as mild or moderate cases and the mortality rate was about 13 per cent; 116 were classified as severe cases and the mortality rate was 45 per cent. The average mortality rate for the two groups combined was 21.5 per cent.

The experience of these men, I must say, was much more similar to my own. I do not think I could find any fractional group of patients with myocardial infarction with a mortality rate of 3 per cent, and because of this I cannot help but question the first series of figures. If you can select the good risk cases as well as Russek and his group did, I would not use anticoagulants in mild cases. If you cannot select them any better than I can, I would suggest that it is desirable to use anticoagulants in every case of myocardial infarction, provided good laboratory control is available.

I think there is a defect in all statistical studies of myocardial infarction, so far as relative mortality rates are concerned. One group of investigators had an average overall mortality rate of 21.5 per cent and the other of 33.4 per cent; one might conclude that the investigators who were less able to discriminate between good risks and poor risks were better able to treat their patients. However, I do not believe this is a justifiable conclusion.

The symptoms which impel patients with myocardial infarction to seek medical care vary widely, and I am sure that some series of cases are much more severe, on the average, than others. Also, the diagnosis of myocardial infarction is often in doubt for some time; all too frequently the diagnosis has to be established more or less by fiat. I get to a point where I say to myself, "I really don't know whether this patient has a myocardial infarct or not, but it looks to me like the chances are best that he has (or hasn't), so I will treat him as if he has (or hasn't) an infarct." The classification of these cases depends largely on the whim of the physician. His results may vary greatly depending on how he classifies the doubtful cases. If he includes many doubtful cases in a series of myocardial infarctions his results may be better than if he includes only clear-cut, and hence more severe, cases.

Contraindications

The first and most important contraindication to anticoagulant therapy, the one that must be emphasized repeatedly, is lack of a laboratory to provide reliable prothrombin time determinations. If you do not have reliable measuring equipment available, I am quite sure you should not use DICUMAROL® or similar anticoagulants.

The second contraindication for use is an erratic or uncooperative patient. Some patients vacillate; one day they feel they don't need the pills, and another day they take more

TABLE 3

CONTRAINDICATIONS TO ANTICOAGULANT THERAPY

1. Lack of a reliable prothrombin time laboratory
2. An erratic or uncooperative patient
3. Prothrombin deficiency (usually with liver disease)
4. Renal insufficiency
5. Ulcers, surgery or trauma
6. Hemorrhagic disease
7. Subacute bacterial endocarditis

than the prescribed amount because of feeling unwell. With such a patient the anticoagulants are so dangerous they are not useful. Another type of patient is not erratic in his cooperation but in his response to the drug, for reasons which are completely unknown. Often it is impossible to know whether a patient is unduly erratic in his response because of metabolic, biochemical and physiologic reasons, or whether he is erratic in using the drug. In either case, anticoagulants are not for him.

The other contraindications are relatively well known and require little comment. I might mention, however, that the evidence contraindicating use of anticoagulants in subacute bacterial endocarditis is not too good. One of the first uses of anticoagulants was to treat this condition with the idea of permitting various antibiotics to penetrate the vegetations on the valve. The mortality rate was considerably higher for patients treated with antibiotics and anticoagulants than for those not so treated. At the time observers thought the reason probably was that the numerous mycotic emboli which have been noted in this disease, mostly in the brain, caused hemorrhage. Our control in those days was not nearly as good as it is now, and therefore I feel that this evidence is a little archaic. However, we are not tempted to return to anticoagulant therapy under these circumstances ordinarily because antibiotic therapy itself has improved so much.

All of these contraindications might be called relative contraindications. Frequently, desperate situations arise where the use of anticoagulants is desirable even though there is increased risk of hemorrhage. I had a patient who had had a peptic ulcer for many years and also had rheumatic heart disease with fibrillation and failure and repeated episodes of pulmonary emboli which were nearly fatal. Some of the latter were showers of small emboli and looked like pneumonia, so that the diagnosis was not made until after he had had eight episodes of pulmonary emboli in 14 months. We gave him anticoagulants in spite of the history of ulcer and for 18 months there were no more episodes of pulmonary emboli. Then he had a gross hemorrhage from the ulcer which had been reactivated, and the anticoagulants had to be stopped. By the time his stools became negative for blood under medical treatment for bleeding ulcer he had another shower of pulmonary emboli and the anticoagulants were started again, whereupon he bled again. I don't know what would have happened eventually—the patient was very uncomfortable with all this and he solved the problem by committing suicide, an effort with which I was somewhat sympathetic under the circumstances. However, I am sure his life was considerably prolonged by the use of anticoagulants, even though their use was attended by great danger.

Control

We are using a prothrombin index to aid in controlling our patients. We measure the prothrombin formation time by the ordinary, quick, one stage method in which the prothrombin time of a normal person is multiplied by 100 and divided by the patient's prothrombin time. The normal time is about 12 seconds; thus, if the patient's time is 12, the prothrombin index or ratio is 100, which is normal; if the patient's time is 24, the ratio is 50; if the patient's time is tripled, the ratio is 33; if it is quadrupled the ratio is 25, and so on.

In a hypothetical, ideal response of the prothrombin ratio to Dicumarol we start with a value of 100. Usually a 300 mg. dose of Dicumarol is given the first day, which reduces the ratio somewhat; on the second day a dose of 200 mg. is given, bringing the index

TABLE 4

$$\text{Prothrombin Ratio} = \frac{\text{Normal Prothrombin Time} \times 100}{\text{Patient's Prothrombin Time}}$$

NORMAL PROTHROMBIN TIME	PATIENT'S PROTHROMBIN TIME	PROTHROMBIN RATIO
12	12	100
12	24	50
13	39	33
12	48	25
12	60	20

down a little more; the next dose is 100 mg., and after that 50 mg. a day will maintain the prothrombin index at about 40, that is, a prothrombin formation time two or three times longer than normal.

Some persons have contended that since this dosage schedule is safe on the average and is so useful it can be used without measuring prothrombin time. That has not been my experience. I wish to discuss some cases which illustrate our experience.

The first case is that of a man 68 years old who had migrating thrombophlebitis and repeated pulmonary infarcts. He had had a fresh pulmonary infarct when I first saw him. As we often do with an older patient, we started with a slightly reduced dose, 200 mg. of Dicumarol, without taking a reading of his prothrombin time. The next morning his prothrombin ratio was about 80, so we gave another dose of 200 mg. His prothrombin index came down still further and he was maintained on about 75 mg. a day. However, presently his prothrombin index rose above the therapeutic range and the dose had to be raised to 100 to 125 mg. a day to bring the index down again. We maintained him on about 100 mg. a day for a time, eventually increasing the maintenance dose to 125 mg. a day. This case illustrates the fact that maintenance doses vary and are not always 50 mg. a day.

Another patient was carried for 12 weeks after discharge from the hospital on a maintenance dose of about 50 mg. of Dicumarol a day. Then he went out of control, his prothrombin time became much too long, and his ratio fell to what we regard as the danger zone. His dose was progressively reduced. He finally got down to a dose of 14 mg. a day instead of the initial 50 mg. Then his prothrombin index rose above therapeutic range and the dose was increased to about 40 to 50 mg. a day. There was absolutely no apparent reason for this deviation. He was in good health and getting along well except for mild angina which he had throughout this course of treatment, although it gradually subsided toward the end. This is a case in which the patient's average requirement was very close to the usual 50 mg. a day, but after three months of excellent response there was an unexpected and unpredictable deviation.

The next patient is typical of the rather sensitive patients whom we encounter frequently. This patient was given an initial

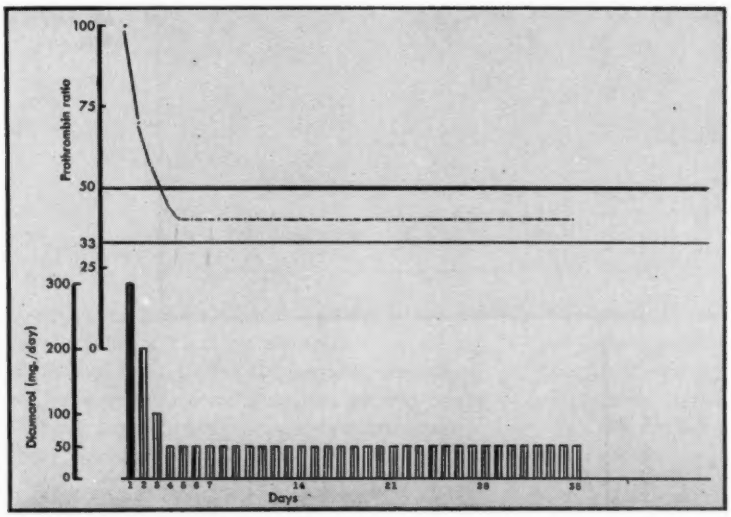

FIGURE 1. Ideal response of prothrombin ratio to Dicumarol.

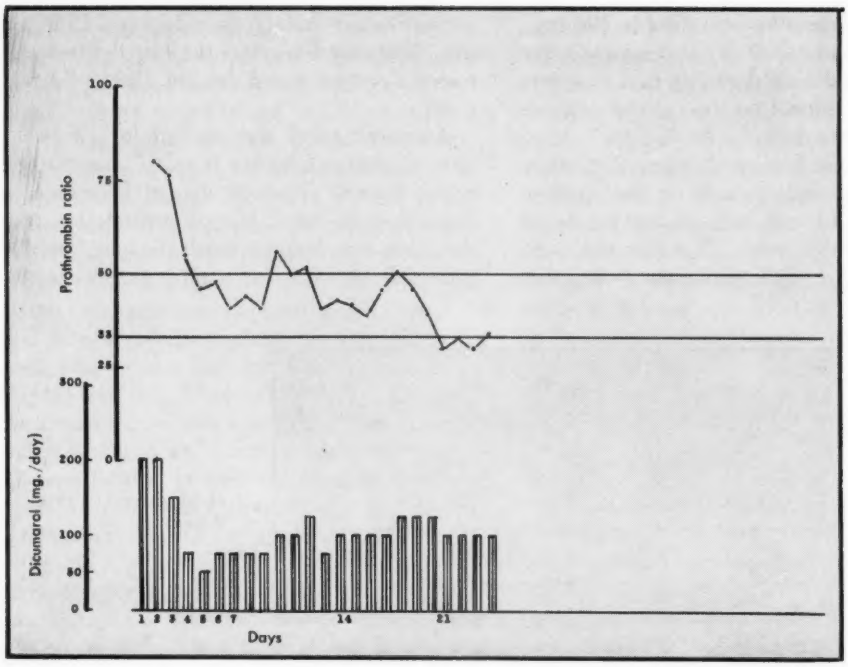

FIGURE 2. Response of prothrombin ratio to Dicumarol in a case of migrating thrombophlebitis and repeated pulmonary infarcts. Patient was a 68 year old man.

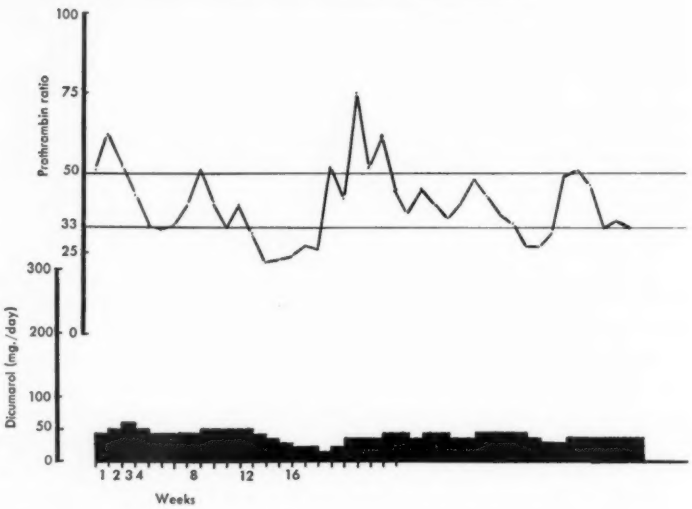

FIGURE 3. Response of prothrombin ratio to Dicumarol, about 50 mg. a day, given as a maintenance dose following myocardial infarction. The patient was ambulatory.

dose of 300 mg. of Dicumarol. The next morning his prothrombin ratio was 52; probably he should have had a smaller initial dose. The second day we gave 150 mg. instead of the usual 200 mg., but that was probably still too much. He went out of control and down into the danger zone where he remained for nine days. During that period the doses were very low, from 0 to 50 mg. a day. Finally we got him back into the therapeutic range and eventually he was fairly well controlled on a maintenance dose of 25 to 30 mg. a day.

These few cases indicate the fact that there are many pitfalls in the use of these drugs.

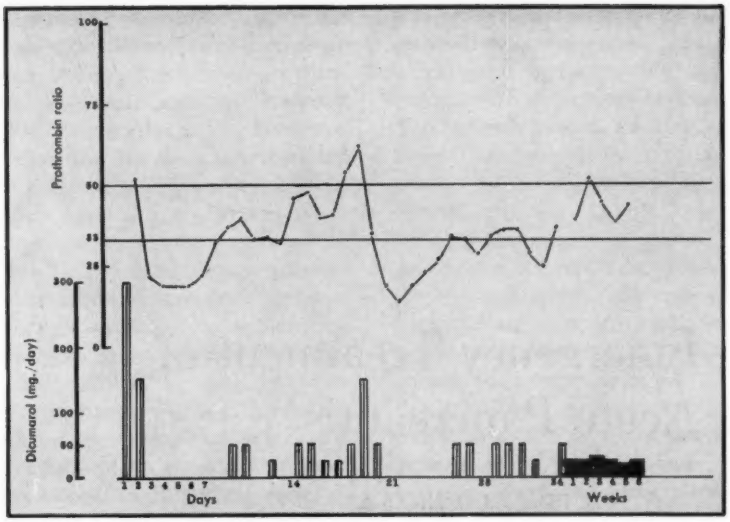

FIGURE 4. Response of prothrombin ratio to Dicumarol in a case of rheumatic heart disease with cerebral embolus.

Great care must be taken in using them and careful control must be maintained over long periods of time. So far the longest time which we have permitted an ambulant patient to go without a prothrombin time determination is three weeks.

Summary

1. Dicumarol is a potent, useful adjunct in the treatment of thrombo-embolic disease.

2. The general fields of its usefulness are well defined.

3. More work is necessary to establish its role in mild diseases and in preventing emboli.

4. The therapy is demanding of the physician from a technical standpoint.

5. A laboratory which provides reliable prothrombin time determinations is essential.

6. Dicumarol can be used only with intelligent, cooperative patients.

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Emergency Treatment of Acute Pancreatitis

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It is remarkable how ideas change completely about the nature of many diseases and how frequently the weight of opinion swings like a pendulum between the extremes of medical and surgical treatment. The average surgeon who must decide on the immediate treatment of such diseases, which have high mortality rates and about which much of the information is vague or conflicting, must evolve his own working plan to meet his responsibility sensibly. He must be familiar with the work of competent investigators, the deductions of responsible authorities and the results of the most experienced clinicians with the disease in question—but this is not all. He must also evaluate properly his own past voyages in the "rough sea" of that disease. His method of treatment of that disease, initiated in the early years of training, must be a pattern altered through his experience and his essential concept of the whole system that disease affects, as well as his own "feel and sight" of the disease itself.

One of the best examples of this type of puzzling and often fatal illness is acute pancreatitis. The change in attitude regarding treatment of this disease is interesting in view of the following facts. As a result of better preoperative preparation and postoperative supports, in addition to safer methods of anesthesia and transfusion and the liberal use of antibiotics, more and more diseases have moved into the surgical column of treatment, as surgical risk in general has decreased. Paradoxically, the position of acute pancreatitis has steadily, over the past 15 years, been shifted so that it is now considered best treated by "conservative means."[1-7] This is paradoxical because acute pancreatitis is "surgical" to the extreme, in that it involves (1) necrosis, (2) hemorrhage, (3) obstruction, (4) ulceration, (5) infection, (6) fluid effusion and distention and (7) peritonitis and (8) is mechanical etiologically,[1,2,8-11] and (9) is etiologically self-perpetuating.[1,12]

It is undoubtedly true that 15 and even 10

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years ago the patients with acute pancreatitis who were operated on immediately died more frequently than those patients not operated on. Understandably, these poor results swung opinion to the conservative side. However, the very fact that this disease was considered an immediate surgical emergency very likely often resulted in hasty surgery under conditions of poor preoperative preparation which do not prevail today. Also, many patients were operated on whose disease from its onset was determinably fatal. Even now there are cases of pancreatitis so acute and overwhelming that neither surgical nor medical treatment results in salvation. We have come to a time to reflect on the degrees of severity of acute pancreatitis and to evaluate properly each disease process, so that each entity is treated according to its suspected pathology—the probability of subsidence as against the possibility of overwhelming toxemia which, if unrelieved, can result in the death of the patient.

The treatment of any disease must be flexible in the light of the altered physiology in its various phases. The basis of pancreatitis is a response by the pancreas to injury, similar to the responses of other abdominal organs. Irritation results (in the majority of cases) from a reflux of bile in individuals having a common channel of biliary and pancreatic ducts, and in whom spasm of the sphincter of Oddi is stimulated.[2] The irritation produces a reactive inflammation with resulting edema, vascular engorgement and exudate which causes swelling of the pancreas, most often in the head. The process may stop there and, if so, the clinical signs are not catastrophic and the serum amylase may be only mildly elevated. This degree of pancreatitis, if limited, often subsides so quickly that the patient is entirely relieved in 24 or 48 hours and refuses further medical care.

However, if edema persists, obstruction of the ducts occurs with pressure and ischemia resulting in necrosis with additional edema, exudate, pressure, ischemia and more necrosis with breakdown of vascular walls and frank hemorrhage. At this point the patient is gravely ill. The pain is so intense that I have noticed a rather constant differential sign, namely, the association of subjective "hysteria" and lack of cooperation with acute upper abdominal pain, severe tenderness and moderate spasm. This hysteric tendency is rarely seen with ruptured duodenal ulcer, intestinal obstruction, acute obstructive cholecystitis or obstructive appendicitis.

When this degree of pancreatitis is present, differential diagnosis is difficult as too often the serum amylase, although elevated, is not higher than in acute peptic ulcer, ruptured peptic ulcer, intestinal obstruction and other causes of peritonitis which demand operation. Of interest in this regard is the paper by Wilson and Seabrook[13] which mentioned reports of high serum amylase in numerous conditions, including pneumonia, splenic trauma, portal or mesenteric thrombosis, chronic alcoholism, carcinoma of the pancreas and acute morphine poisoning. These authors also reported 10 patients with elevated serum amylase who came eventually to surgery or autopsy. Only three of these were found to have acute pancreatitis. One case ended fatally because surgery was withheld under the diagnosis of acute pancreatitis and at autopsy a perforated peptic ulcer was found. In addition, it should be kept in mind that the shock of other abdominal catastrophes may result in urinary retention which again results in misleading high amylase reports.[14]

On the other hand, conditions occur in which the very virulence or duration of the pancreatitis results in low serum amylase values which are readily misinterpreted.[1,3,15] To depend on one laboratory test with its variables from venipuncture to chart recording seems unwise in the light of the available preoperative supports and the short operation necessary "to be sure," which will also relieve the conditions present. However, even at this point it is prudent to use transfusion for incipient shock, oxygen for collapse, antibiotics, sedation and relaxing drugs such as atropine and papaverine—and to observe the patient a few hours longer. If, however, the patient does not at least "hold his own" in the face of advancing inflammation, distention and rupture of the pancreatic ductules, surgical relief

becomes necessary. The toxemia causing death from an enzymatic peritonitis must be avoided and this can be done by (1) draining the exudate out of the abdomen and (2) relieving the tension from the biliary tree.

This is not a formidable operation and can be done with dispatch. A right upper quadrant incision will immediately disclose the pathology, ending the guessing game. The patient under anesthesia and fully oxygenated, with whole blood flowing in his veins, atropinized and with gastric suction in place, is briefly and limitedly explored. If pancreatitis is not present, the surgeon can correct whatever mechanical abnormality is present, and if hemorrhagic pancreatitis is found, a cholecystostomy or choledochostomy may be of great value. In this manner, treatment is directed toward what is, at least, the most accepted etiology of this disease. A second large drain to the pancreas allows egress of the lethal and shocking fluid rapidly accumulating within the peritoneal cavity.

In light of the objectives to be achieved, there can be little objection to this limited surgery. With modern methods of anesthesia, the surgeon is continually alerted to the patient's condition and with this in mind, along with his findings at laparotomy, he can rapidly determine the extent and duration of the operation. Meanwhile the patient *is* being treated medically. Alternatively, without relief of biliary tension or drainage of the peritoneal hemorrhage and exudate, no medical treatment may suffice (unless the process itself is self-limited) to correct the vicious circle of edema, obstruction, necrosis, hemorrhage and enzymatic peritonitis. This is the headlong path of pancreatic inflammation even when the disease starts in the isolated portions of its aberrant rests.[16]

Secondary results may rapidly ensue, adding the factors of fat necrosis and retroperitoneal spread of edema and necrosis along the aorta and iliac vessels. Spontaneously converted trypsinogen reacts with itself to form more active trypsin, breaking down more tissue protein and fat. The bloody exudate irritates the gastrointestinal tract to an obstinate paralytic ileus, increasing the general toxemia. The paralytic ileus itself often leads to pleural effusion or pulmonary atelectasis. The released fatty acids combine with calcium ions, which may bring the serum calcium to tetany levels. Cardiovascular effects of hemoconcentration and decreased blood volume are also difficult to control with continuing enzymatic peritonitis, which may gradually bring the patient to irreversible shock.

With the above factors in mind, 22 patients with acute pancreatitis were observed in a 10 year period, from 1945 to 1954. Of these patients, 9 underwent surgery and 13 were treated medically. There were no deaths. I believe that the experience of a small community hospital is important in evaluating surgical statistics, and so I hope that the following case reports will be of interest, particularly in comparison with reports from larger, more specialized hospitals. The number of these cases in relation to total hospital admissions emphasizes the scarcity of this disease recently noted by Bockus,[1] who reported an incidence of 0.05 per cent in 70,000 admissions. The 22 cases of this report were the total out of 45,000 admissions to the Kadlec Hospital, of which the first 10 cases were diagnosed and treated by me from a total of 5100 personal admissions to the same hospital. This infrequency, compared with the much more common occurrence of simulating abdominal disorders which unquestionably demand surgery, points again to the danger of adhering rigidly to a medical plan of treatment for cases diagnosed as possible acute pancreatitis.

The patients treated by surgery will be described first, and it will be noted that in this group the diagnosis was certain because it was made by direct inspection. The second group comprises those treated medically, and here not only is the diagnosis questionable, but the patients were undoubtedly undergoing an ultimately milder process whose fortunate outcome was as likely due to a self-limited process as to the specific treatment.

Cases Treated Surgically

Case 1—The 34 year old wife of a staff physician was admitted to the hospital on

March 8, 1947. One hour following a large meal she suddenly felt very severe epigastric pain radiating to the umbilicus and back, associated with deep nausea and profuse vomiting. A neighbor called the ambulance and the patient was faint, weak, cold and perspiring on arrival at the hospital.

I saw her in the emergency room and found her doubled up in a jackknife position, unable to cooperate in giving a history or in physical examination. There was marked shock. Her skin was cold and clammy, her pulse rapid and thready and only a systolic pressure of 60 was obtainable. The abdomen was boardlike and tenderness severe in the epigastrium. She could not breathe deeply, cough or change position because of the severe pain. Liver dullness was present. Her temperature was subnormal, white blood count 15,000 with 97 per cent polymorphonuclear cells. A flat plate of the abdomen showed no free air in the subphrenic regions. Wangensteen suction and intravenous fluids and penicillin were started.

She was observed for seven hours, during which heavy sedation was necessary to relieve the pain. Nevertheless, her temperature rose, her pulse became weaker and abdominal distention commenced. Because the abdominal catastrophe apparently was continuing, I decided on laparotomy to treat a possible ruptured ulcer or a rapidly compromising intestinal obstruction. If acute pancreatitis was present, I felt that it was of such a fulminating nature that the shocking peritonitis must be relieved.

Accordingly, I made a right rectus incision while a supportive transfusion was administered. A large amount of bloody fluid was found in the abdomen, and the duodenum was covered with a thin but profuse bright red, filmy exudate which spread out on the posterior parietal peritoneum to include the head and almost half the body of the pancreas. The pancreas was markedly hardened, enlarged and reddened. Fat necrosis was seen as numerous white opaque plaques resembling candle grease about the peritoneum, surrounding the pancreas and duodenum. The gallbladder was normal, as were the biliary ducts. The area about the pancreatic capsule was drained and the abdomen closed in layers.

During the first two days following the operation her pulse remained rapid and her abdomen distended despite profuse drainage; however, there was no recurrence of the severe pain. Intravenous fluids were continued until the fourth postoperative day when the patient was able to tolerate a soft bland diet. (Further transfusions and 400,000 units of penicillin were given daily.) On the third postoperative day, the blood sugar was 87, the blood calcium 9.5 and the serum amylase 300 mg. per cent. From then on convalescence was rapid. There has been no recurrence.

Case 2—A 23 year old white laborer was admitted to the hospital on July 21, 1947 with the chief complaint of intense midabdominal pain and vomiting of six hours' duration. A similar, less severe attack had occurred approximately one month earlier. The past history was significant; he had suffered severe trauma to the left kidney and spleen in an alcoholic brawl. He awoke in jail and was moved to a hospital where a splenectomy was performed. A two month stormy convalescence followed. During the next three years he got drunk frequently.

The patient was an obese young man, markedly anxious and perspiring freely. He complained bitterly of severe abdominal pain, was often incoherent and uncooperative. The abdomen was slightly distended, tender in the epigastrium and both upper quadrants, and following sedation a fluid wave could be felt. The white blood count was 16,900 with 87 per cent polymorphonuclear cells. A flat plate of the abdomen revealed no free air under the diaphragm and a questionable loop of dilated small intestine (figure 1). A Miller-Abbott tube was passed, intravenous fluids and penicillin started and observation continued for eight hours. During this time he vomited repeatedly, despite continuous suction, his color became poor, his skin cold and clammy and the pain remained severe despite sedation.

Although the serum amylase was 1000 mg. per cent, laparotomy was scheduled as it was felt that probably a primary or coincidental mechanical intestinal obstruction from adhe-

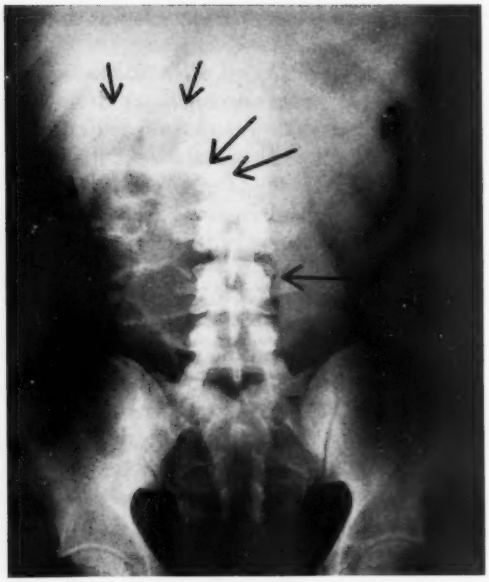

FIGURE 1. Roentgenogram strengthens clinical diagnosis of intestinal obstruction (concomitant with pancreatitis?) in case 2.

sions of the previous splenectomy was not being relieved under conservative treatment. In addition, it was apparent that acute pancreatitis, which was more likely, was of a fulminating nature which, through abdominal effusion, had caused more marked distention, dyspnea, cyanosis and increasing shock.

With transfusion and mask oxygen as aids, I opened the abdomen under spinal anesthesia and aspirated 1500 cc. of bloody fluid from the abdominal cavity. Fat necrosis was marked throughout the omentum and mesentery. The duodenum and pancreas were covered with a red glossy exudate and the pancreas was enlarged and friable. The gallbladder was markedly distended but contained no stones. A cholecystostomy was quickly performed using a Mayo drain and the pancreas was extensively drained without incising it. The abdomen was then closed in layers.

A stormy convalescence followed with bilateral pneumonitis and cardiac failure developing as complications. Intensive cardiorespiratory and antibiotic treatment eventually were successful and the patient was discharged on his twentieth postoperative day. During the immediate postoperative period the abdominal drainage was profuse, mucoid and recurrently hemorrhagic to a moderate degree. On the third, fourth and eighth postoperative days the serum amylase was 643, 224 and 124 mg. per cent respectively.

Case 3—A 41 year old white man was admitted to the hospital on March 18, 1952 with the chief complaint of sudden severe abdominal pain while at home convalescing from a subtotal gastrectomy which I had performed 10 days before. His postoperative course following the stomach resection had been smooth and he had been up and about with no major complaints.

Soon after the abdominal pain started he was taken to the hospital and when seen in the admitting room he was in definite shock and severe pain. Abdominal examination revealed the retention sutures in place on the fresh uninfected wound. The abdomen was extremely tender, especially on the left side. There also was tenderness of both lower quadrants and dullness in the flanks, presumably due to fluid spillage. Plasma infusion was started, morphine sedation given, transfusion arrangements made and the patient was dispatched directly to the operating room with a diagnosis of sudden rupture of the duodenal stump.

With Wangensteen suction in place, transfusion and oxygen forced, intubation ready and atropinization effected, laparotomy was begun under spinal anesthesia. Two liters or more of hemorrhagic fluid were immediately encountered and drained. The duodenal stump was inspected and found to be securely closed. The pancreas was markedly swollen and reddened and fat necrosis was widespread. The pancreatic capsule was drained without incision and the abdomen quickly closed as one layer. The patient was kept in the operating room for vigorous antishock treatment for some time after the 35 minute operation. His blood pressure gradually rose to 100/60 and he was taken to the ward in poor condition.

During the next few hours and under continuous transfusion, his blood pressure rose to 150/80. There was never a return of shock

and the pain was never severe again. Abdominal drainage was profuse until the third postoperative day when it practically ceased. At this time his serum amylase was 303 mg. per cent. Convalescence was prolonged because of the severe debilitation and the patient was discharged one month later, gaining steadily in weight and strength. There has been no recurrence.

Case 4—A 53 year old white bus driver with a history of chronic alcoholism was admitted to the hospital on August 30, 1952 with upper abdominal pain of seven hours' duration. During the preceding three hours severe nausea and vomiting had begun and persisted to admission. Past history indicated chronic, low-grade abdominal pain accompanied by backache, bloating and a feeling of fullness. There had been no previous acute attacks with pain similar to that present on admission.

The examination disclosed an obese white man with mild cyanosis, marked anxiety and moderate shock. Epigastric pain and tenderness were severe. The abdominal flat plate was clear and the white blood count 16,600 with 93 per cent polymorphonuclear cells. As the pain was more severe very high in the epigastrium and left lower chest and dyspnea and cyanosis accompanied the pain, an electrocardiogram was taken immediately, which showed no abnormalities. Morphine and atropine were given and intravenous fluid, 5 per cent glucose in distilled water, was started. Penicillin and streptomycin were also administered. Despite frequent sedation, Wangensteen suction and atropine, the pain, cyanosis and dyspnea increased.

With whole blood available, the patient was operated on with the diagnosis of acute hemorrhagic pancreatitis. This was found, in combination with profuse bloody exudate and fat necrosis. The gallbladder showed chronic inflammation but no stones. This organ was drained and the cholecystostomy was supplemented with wide pancreatic drainage. For the first three days the abdominal drainage was moderate and the pain minimal except for discomfort from abdominal distention. The patient was given whole blood transfusions daily for three days in addition to other intravenous fluids. A serum amylase was not taken until the third postoperative day at which time it was 75 mg. per cent. The cholecystostomy tube drained well at all times and was removed on the ninth postoperative day, two days after the frequently shortened Penrose drains were removed. The patient was discharged ambulatory on the twelfth postoperative day. There has been no recurrence.

Case 5—A 52 year old white man was admitted to the hospital on February 1, 1953 with a history of severe acute upper abdominal pain of several hours' duration. He had had similar attacks for three years but of a milder degree. On admission the patient was vomiting and pale and his skin was cold and damp. The abdomen was spastic and the epigastric tenderness severe, causing direct backache on palpation. The history of past possible peptic ulcer associated with the sudden abdominal pain led to a diagnosis of perforating peptic ulcer. A flat plate of the abdomen showed no free air under the diaphragm. The white blood cell count was 23,700 with 86 per cent polymorphonuclear cells.

Soon after admission, DEMEROL® sedation, Wangensteen suction, penicillin and intravenous fluids were administered. The pain subsided and observation continued overnight. During the early morning hours the pain and shocklike episode recurred and persisted. Accordingly, the patient was transfused and brought to the operating room. Laparotomy disclosed over a liter of bloody fluid in the abdomen and widespread fat necrosis. The pancreas was massively involved in inflammation. The gallbladder was distended but free of stones. The lesser sac was widely drained and a rapid cholecystostomy performed. The patient awoke without severe pain. Convalescence was smooth with the abdominal drainage profuse for two days. He was up and about and tolerated a soft diet on the fourth postoperative day and was discharged on the seventh postoperative day with gallbladder tube and skin sutures still in place. Sutures and tube were removed after the second week with complete and rapid healing.

Case 6—A 34 year old white woman with

an eight year history of recurrent attacks of right upper quadrant and epigastric pain, accompanied by nausea and vomiting, was admitted to the hospital March 24, 1946. During the previous week the abdominal pain had been unusually persistent but relief followed conservative measures soon after admission. In the course of observation and cholecystography, pain recurred and jaundice appeared. Two days after admission sudden epigastric and back pain returned, more severe than usual. Her temperature was elevated, prostration evident and abdominal tenderness severe. Sedation, infusions and penicillin were administered but the pain increased in intensity. The icteric index was 50 units. A diagnosis of common duct obstruction was made and surgery advised.

Free amber fluid was encountered. Exploration revealed the gallbladder as a thick small structure containing numerous calculi. The fundus of the gallbladder adhered densely to the prepyloric portion of the stomach where a cholecystogastric fistula had occurred. Several stones were palpated in the stomach. This portion of the pathology was of a chronic nature. A more acute process was seen in the pancreatoduodenal area where glossy edema and redness were marked. The gallbladder was removed, the stones were evacuated from the stomach through the fistula opening, and the stomach walls were then refreshed and closed. The enlarged common duct was explored and a large calculus removed from its distal portion. A T tube was placed in the common duct and the areas of Morison's pouch and the head of the pancreas were drained.

The patient had a satisfactory convalescence with rapid subsidence of jaundice. A cholangiogram taken on the eighth postoperative day showed the dye entered easily not only the duodenum but also both pancreatic ducts (figure 2).

Case 7—A middle-aged white woman was admitted to the hospital on April 6, 1950 for treatment of severe right upper quadrant pain. A cholecystectomy for cholelithiasis six months previously had not relieved the pain. At that time the common duct was explored, several calculi removed and T tube drainage instituted. On admission, the abdominal wound was well healed but there was tenderness in the epigastrium with moderate spasm. The hemoglobin was 13.5 gm., the red blood count 5,200,000 and the white blood count 7200 with 63 per cent polymorphonuclear cells. The icteric index was 17 units, the alkaline phosphatase 20.8 units. The total protein was 8.68 per cent. As part of the diagnostic work-up, a gastrointestinal series and a barium enema were done and no abnormalities found. The pain recurred in severe attacks accompanied by nausea and the patient appeared listless and apathetic.

Four days after admission, following repeated attacks, the patient was brought to the operating room and the abdomen explored under fractional spinal anesthesia. A moderate amount of brown fluid was found in the peritoneal cavity and the pancreas was reddened and markedly enlarged and hardened by glossy edema. The pancreatic capsule was studded with many white opaque spots. The common duct contained no stones and was

FIGURE 2. Cholangiogram visualizing both pancreatic ducts in case 6.

markedly enlarged. On opening this structure difficulty was encountered in entering the duodenum with a Bakes dilator. Dilation was systematically performed, increasing the size up to the largest dilator, followed by a curved stone-retrieving clamp which was forcibly opened while hugged by the sphincter of Oddi. In this way this sphincter was markedly stretched and remained atonic. The pancreatic capsule and Morison's pouch were drained by Penrose drains brought out separately from the T tube in the common duct. The abdomen was closed in layers. The patient tolerated the procedure well and was returned to the ward in good condition.

The postoperative course was relatively smooth, although there was profuse viscid and biliary drainage during the first five days following operation. Following this, the drainage lessened and the Penrose drains were removed on the ninth postoperative day. She was discharged improved with the T tube in place two days later. The T tube was removed after one month; its tract healed promptly. There has been no recurrence.

Case 8—A 35 year old white housewife was admitted to the hospital on May 4, 1950 with severe epigastric pain. She had had numerous similar attacks during the preceding five years but these were more definitely biliary colic with right upper quadrant pain radiating to the back and right scapular region, accompanied by nausea and vomiting and on one occasion light transient jaundice. She had been observed over the years for gallbladder disease but x-rays of this organ were repeatedly normal. On consultation, three months before this admission, I had noted that the biliary ducts (with no special technic of cholangiography) were unusually well visualized (figure 3). I had re-examined x-rays taken three years before which also "coincidentally" visualized the biliary ducts. A diagnosis of biliary dyskinesia was made at that time and, considering the unrelieved recurrent symptoms, surgical treatment was suggested, but refused.

Soon after arriving at the hospital the patient was seen in the emergency room. The attack had subsided spontaneously. She was admitted for further study. The pain recurred the same evening but was relieved by sedation. The next evening pain recurred with increased intensity, centered in the epigastrium and boring to the back. Vomiting recurred throughout the evening. Following sedation, infusion was begun, a Levin tube passed and Wangensteen suction applied to the stomach.

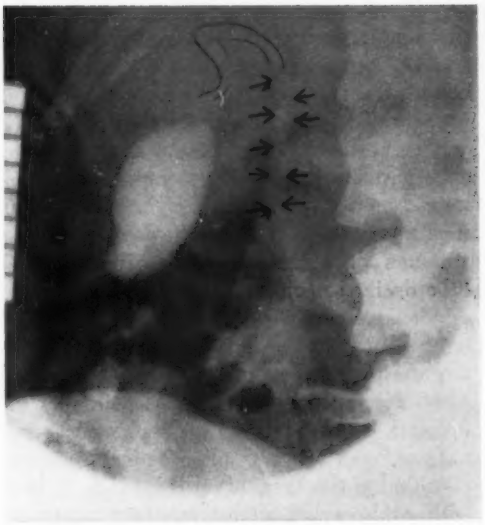

FIGURE 3. Biliary duct visualization in case 8 which was present at each of three *routine* cholecystographies done years apart. The visualization excited suspicion of spasm of the sphincter of Oddi.

Early on May 6, 1950, with transfusion in place, laparotomy was performed under PENTOTHAL® sodium and curare anesthesia. A large amount of murky fluid was noted in the abdomen accompanying acute inflammation of the pancreas. The gallbladder appeared normal and contained no stones. The common duct was dilated to approximately three times its normal size. The patient tolerated the operative procedure well and the common duct was opened accordingly. Obstruction was encountered at the sphincter of Oddi but a small Bakes dilator could be admitted through it into the duodenum. With this probe in the intestine as a guide, the duodenum was opened vertically and the sphincter of Oddi sectioned. A long Cattell T tube was then

placed in the common duct and threaded through it, well into the duodenum (figure 4). The opening in the duodenum was then closed transversely. The pancreatic capsule was drained and the abdomen closed in layers.

The postoperative course was stormy despite gastric suction and accompanied by prolonged nausea and vomiting. Parenteral feedings were necessary for eight days, and large amounts of antibiotics were given. The T tube drained profusely a mixture of bile and duodenal contents and was removed on the tenth day. By the fourteenth postoperative day the patient was up and about, tolerating a soft diet well, and was discharged from the hospital. There has been no recurrence.

Case 9—A 39 year old white mechanic was admitted to the hospital on December 2, 1952 with a history of almost constant upper abdominal pain of two months' duration, often dulled by the ingestion of large amounts of alcohol. On the day of admission the epigastric pain was especially severe and accompanied by profuse vomiting. Jaundice had been deepening over the preceding month. He had been hospitalized for nine days of the preceding month and observed for anorexia, abdominal pain and jaundice. Examination at that time revealed a tender mass in the upper abdomen. (Subsequent history from relatives indicated that the patient had been on a prolonged alcoholic bout following an acute abdominal episode in which he had collapsed and suffered the symptoms of shock.)

On that first admission the icteric index was 275 units and the BROMSULPHALEIN® test showed less than 6 per cent retention after 45 minutes. The stool was positive for occult blood on three occasions. The thymol turbidity and cephalin flocculation tests were normal. Roentgenographic work-up failed to visualize the gallbladder and indicated a mass was present in the region of the head of the pancreas (figure 5). Since at that time I did not know of the earlier acute episode, I suspected a neoplasm in the head of the pancreas. However, the patient refused exploration and insisted that he be permitted to leave the hospital on November 19, 1952.

Following readmission on December 2,

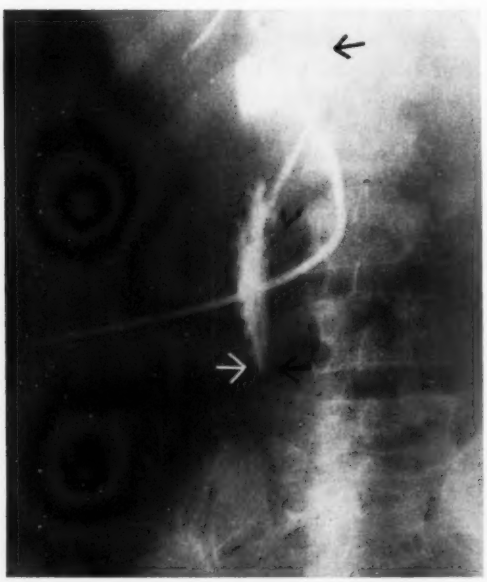

FIGURE 4. Cholangiogram showing long Cattell T tube through ampulla of Vater in case 8.

FIGURE 5. Evidence of pancreatic enlargement in case 9.

1952 the pain was relieved by sedation and a flat plate of the abdomen showed no air under the diaphragm. A transfusion was started, Levin tube and gastric suction applied, large dosages of vitamin K were administered and laparotomy performed under continuous spinal anesthesia. The abdominal findings were extensive. Approximately 1 liter of blood-tinged fluid was found free in the peritoneal cavity. A tumor extended from the head and neck of the pancreas and pressed around and above the second portion of the duodenum, intimately involving the superior mesenteric artery and vein. The abnormal tissue also extended under the duodenum in the area of the common duct, which appeared to be completely obliterated by the pathologic process. The tumor mass swelled the pancreas to approximately four times its normal size, and extended to the lesser sac but did not incorporate it, as a pseudocyst does.

The consistency of the mass was not that of a carcinoma and biopsy showed only necrotic tissue within fat necrosis in adipose tissue. The pathologist was kind enough to scrub up and palpate the mass in vivo but could not be certain that it was benign. The omentum was thickened and hardened in many areas, as with either metastatic involvement or fat necrosis. The bulk of the omentum was extreme as was the other intra-abdominal fat, due to the obesity of the patient. The gallbladder was thickened but distended nevertheless, and contained no stones. It was felt that since the mass was not that of a pseudocyst and since it virtually obliterated the common duct, it must be attacked in the same way as would an obstructing and possibly malignant tumor.

In preparing to excise the head and neck of the pancreas and common duct, the stomach was mobilized, its lower third divided and this portion, with the pylorus, was resected, the duodenum being dissected subserously almost to the ligament of Treitz.[17] The head and neck of the pancreas, or what replaced the pancreas, were removed as far as possible. Because of the friability of the diseased tissue it was possible to clean it off the mesenteric vessels by blunt dissection. Excised material consisted of the stomach, duodenum, head and neck of the pancreas and the common duct. The latter was never distinguishable as such because of its severe involvement in the disease process. Reconnections were made, after closing the duodenal stump just proximal to the ligament of Treitz, by bringing the jejunum in an anterior loop anastomosis to the stomach and anastomosing the gallbladder to the jejunum approximately 4 inches lower on the same loop. Penrose drains were used both from the duodenal stump and from the pancreatic stump, which was covered by the mobile remaining duodenal serosa.

Although the operation consumed five hours, the general condition of the patient remained fair, sustained by 2500 cc. of whole blood transfusions. Near the final stages it was necessary to complete the procedure rapidly as the blood pressure remained precariously low during the last 45 minutes. For this reason a clearer picture of the upper common and pancreatic ducts could not be obtained. Neither gross nor histologic examination of two large irregular specimens (one 4.0 by 5.0 by 5.5 cm., the other 6.0 by 5.0 by 7.0 cm.) and other numerous small specimens showed neoplasm, although fat necrosis was widespread. The stomach and duodenum were likewise free of cancer.

Although the postoperative course was stormy, the blood pressure rose when the patient returned to his room and was sustained by further transfusions. He was treated thereafter under a special nurse regimen, oxygen tent control, parenteral feedings and large doses of TERRAMYCIN® intravenously, as well as penicillin and streptomycin intramuscularly. The most serious postoperative complication was persistent delirium tremens which was difficult to control. The jaundice subsided rapidly; the drainage lessened after three days to viscid spotting which continued for four weeks after discharge on the twentieth postoperative day. Since then, although the patient has continued his alcoholic routine (including clinic-visiting days), there has been no recurrence of abdominal pain and drainage or jaundice. He has gained 30 pounds since discharge.

Comment

In treating the patients described an attempt was made to relieve the dynamic aberrations in physiology noted at the patient's bedside rather than on the basis of a specific diagnosis dictated from the laboratory. In each instance differential diagnosis was considered from the standpoint of eventual outcome, and although medical management was quickly instituted, surgical alternatives were prepared concomitantly. In each instance surgery was done on an emergency basis to interrupt and relieve the accumulative effect of self-perpetuating pathology. At any point in the early course of the disease, evidence of recovery or satisfactory response to medical treatment would have resulted in the continuation of this conservative regimen.

It should also be noted that the extent of surgery varied and depended on (1) the intra-abdominal findings and (2) the patient's condition during the operation. The laparotomy findings were viewed with the primary aim of relieving the peritoneal chaos by drainage and secondary aim of correcting any obvious etiologic fault. The latter objective necessarily had to be balanced against the patient's ability to tolerate the surgical procedure needed. Therefore, in the first case the poor condition of the patient and the normal extrapancreatic findings indicated that simple peritoneal drainage alone should be instituted. In case 2 the same was true except that the obvious increased biliary tension was also relieved by a rapid cholecystostomy. In case 3, a ruptured duodenal stump was suspected in view of the recent duodenal surgery. The laparotomy findings, however, directed the course of simple pancreatic drainage.[18] Cases 4 and 5 were treated similarly to case 2 for the same reasons.

In the last four cases the findings of acute pancreatitis were intimately involved with more marked gallbladder and bile duct pathology. In each case the patient's condition was good enough and the preparations thorough enough to permit the indicated surgery. Thus in case 6 the cholecystogastric fistula was treated by cholecystectomy and closure of the gastric aperture and the common duct was cleaned of calculi and drained. In cases 7 and 8 a direct approach was made to atonize the sphincter of Oddi.

In case 9, although the patient's condition was not good, the intra-abdominal pathology found left no alternative (especially as regards jaundice with an obliterated common duct which has been previously noted in acute pancreatitis)[19] but to proceed to the removal of the peculiar mass and finally to reconstruct biliary and gastrointestinal channels.

The final results in these cases have unquestionably been satisfactory. It is impossible to know what would have resulted had nonsurgical treatment been continued in each case. Certainly at the time surgery was scheduled the response to medical treatment had been poor and in most instances the outlook appeared grave. In cases 6, 7, 8 and 9 surgical treatment was inevitable and fortunately definitive measures could be taken at the same time that pancreatic pressure was released. In case 9 it is interesting to speculate whether the extensive surgery would have been necessary if the patient had been seen and treated within the first 24 hours or so of his acute illness.

The first four cases were so acute clinically that I would have been less surprised to find a ruptured hollow viscus than acute hemorrhagic pancreatitis. A possible indication of the ultimate course in patients under continued medical measures is suggested by the following case reported by Gambill et al.,[20] in which these investigators had an unusual opportunity to study the numerous complications, both clinical and chemical, which occur in fatal pancreatitis.

A man, aged 55, was hospitalized because of severe abdominal pain of 30 hours' duration. In the preceding 10 years he had had about six such episodes. There were skin pallor, profuse perspiration, dark urine, nausea and vomiting, abdominal distention, spasm and tenderness. About 48 hours after the onset of the attack the serum amylase value was 2,666 units. On the fourth day the blood urea was 168 mg. per 100 cc. and the fasting blood sugar was 340 mg. per 100 cc. By the sixth

day ascites and abdominal distention had increased and four loose bloody stools were passed. The serum amylase had decreased to 160 units. On the eighth day the serum calcium was 5.7 mg. per 100 cc. Subsequently there was increasing abdominal distention and ascites, and hydrothorax became apparent. Large amounts of fluid were removed by paracentesis. Increased blood urea and sugar concentrations and low serum calcium and potassium values persisted. Urinary output decreased to a low level and there were signs of respiratory and cardiac embarrassment and increasing toxemia. Death occurred on the seventeenth day of the attack.

Autopsy revealed acute hemorrhagic pancreatitis with disseminated fat necrosis and calcification, generalized peritonitis, ascites, acute cholangitis, cholelithiasis, bilateral hydrothorax and atelectasis of the lungs.

Cases Treated Medically

Case 1—A 63 year old white man was admitted to the hospital on October 8, 1946 with severe abdominal pain. Approximately 24 hours previously he had fallen hard, striking his upper abdomen on the sharp corner of a wooden counter, and had immediate severe abdominal pain and faintness. The pain subsided slowly but never disappeared. Three hours before admission epigastric pain suddenly became as severe as during the initial trauma. There was severe vomiting and the patient was brought to the hospital in shock. Examination revealed a moderately obese man, ashen-colored, cold, clammy and severely tender in the epigastrium and umbilicus. Flat plates of the abdomen showed no abnormality. The white blood cell count was 22,000 with 91 per cent polymorphonuclear cells. There was a 2 plus sugar on urinalysis and the blood amylase was 1,020. The icteric index was 12 units.

The patient was carefully observed under Demerol sedation. He was given penicillin and gastric suction and intravenous fluids were begun. Blood transfusion was kept in readiness. During the next few hours he improved remarkably and although pain recurred, it was not accompanied by shock or severe abdominal signs. By October 10 the serum amylase had dropped to 197 mg. per 100 cc. and the blood calcium was 9.43 mg. per 100 cc. Abdominal ache continued for three days but at no time was there any sign of progressing illness. A soft diet was tolerated on the fourth day following admission and a slow but sustained recovery resulted in discharge on the twelfth day.

Case 2—A 12 year old white boy was admitted to the hospital on January 7, 1948 with upper abdominal pain, nausea and profuse vomiting. He had been convalescing from mumps and all parotid swelling had subsided the night before the abdominal pain began.

On admission his skin was moist and cool, his pulse thready. Epigastric tenderness and spasm were marked. The white blood count was normal but the serum amylase was 486 mg. per 100 cc. Stools were negative for gross or occult blood. Soon after admission the pain subsided gradually; color, pulse and blood pressure returned to normal. Two days after admission only mild tenderness persisted over the pancreas, a bland diet was well tolerated and the patient was discharged the next day.

Case 3—A 26 year old white man with a past history of chronic alcoholism was admitted to the hospital on May 10, 1949 for relief of severe upper abdominal pain which had started immediately after a large meal and continued almost unabated for five hours. Nausea and vomiting persisted until mild hematemesis occurred. On examination circulatory collapse was evident in the cold, moist skin. There was faintness which increased on palpating the exquisitely tender supra-umbilical area. An electrocardiogram was negative. The white blood count was 14,150 with 61 per cent polymorphonuclear cells and the flat plate of the abdomen showed several loops of dilated small intestine. The serum amylase was 751 mg. per 100 cc.

Treatment consisted of passage of a Miller-Abbott tube after Demerol and atropine sedation. Gastric suction was continued while fluids were given parenterally. Penicillin and streptomycin were also started and nasal oxygen and transfusion prepared. The patient was then carefully observed and although ab-

dominal pain and vomiting continued, all signs of circulatory collapse disappeared. Medical treatment was therefore continued and within 48 hours pain became minimal, food was well tolerated and the patient was allowed out of bed. He was discharged two days later with no further incident of pain.

Case 4—A 41 year old white man was admitted to the hospital on March 21, 1949 with a history of sudden onset of severe epigastric pain of eight hours' duration. Continuous nausea and vomiting accompanied the abdominal pain. He had had previous less severe attacks. On examination he appeared acutely ill, dyspneic and moderately hysteric with pain. The abdomen was exquisitely tender in the epigastrium and moderate spasm was present. The white blood cell count was 13,000 with 86 per cent polymorphonuclear cells. Flat plates of the abdomen and an electrocardiogram showed no abnormalities. The serum amylase was 202 mg. per 100 cc. He was treated with repeated doses of atropine, SODIUM LUMINAL® and codeine sulfate. Nothing was given by mouth and the patient was observed through the night. The pain was relieved several hours after admission and did not recur, although abdominal tenderness remained until discharge on March 24, 1949.

Case 5—A 33 year old white laborer was admitted to the hospital on April 20, 1950. He had had episodes of right upper quadrant pain for over two years. Several days before admission recurrent severe pain began in the upper abdomen and increased in intensity, persisting through the entire day of admission. There had also been severe vomiting. On examination there was nausea, repeated retching and an appearance of anxiety. Supraumbilical tenderness was severe and spasm marked. The white blood count was 11,550 with 92 per cent polymorphonuclear cells. A flat plate of the abdomen showed no free air under the diaphragm and no opaque calculi in the region of the gallbladder. The serum amylase was 307 mg. per cent and the cephalin flocculation test negative in 24 and 48 hours.

The patient was observed closely over the next 10 hours and treated with repeated doses of codeine and atropine for pain. Penicillin and streptomycin were given and intravenous fluids started. By the next morning the patient's condition had improved markedly. Repeated serum amylase tests showed gradual reduction during the five days following admission. A bland diet was well tolerated on April 23 and was continued to the day of discharge, May 5, 1950.

Case 6—A 48 year old obese white woman was admitted to the hospital on April 9, 1949 for treatment of severe upper abdominal pain radiating to the right scapular region. The history indicated that she had had acute cholecystitis 10 years previously and a cholecystostomy was done at that time. Since then recurrent epigastric and right upper quadrant pain had occurred frequently, usually after a heavy meal. There was no history of definite jaundice or weight loss.

On admission the patient complained of epigastric pain and vomited repeatedly. There was marked anxiety and her skin was moist and pale, although her pulse was strong and regular at 80 with the blood pressure 110/70. The white blood cell count was 18,650 with 83 per cent polymorphonuclear cells and the serum amylase 1,317 mg. per cent. Abdominal x-rays showed no free air under the diaphragm, but several dense shadows were interpreted by the roentgenologist as "possible pancreatic calculi." A cholecystogram taken later failed to visualize the gallbladder.

The patient was carefully observed and although the abdominal pain, nausea and vomiting continued, they showed no progression of the pathologic process and there was no further evidence of circulatory collapse. The treatment consisted mainly of sedation with atropine and 30,000 units of penicillin every three hours. The elevated temperature, white blood cell count and serum amylase all gradually subsided concomitantly with relief from pain. The serum amylase levels fell to 578, 561, 474 and 348 mg. per cent on April 12 through April 15. A bland diet was well tolerated by the seventh day following admission when, at the patient's insistence, she was discharged on a reducing diet and advised to return for definitive surgery at a later date.

Case 7—A 50 year old man was admitted

to the hospital on March 9, 1954 with severe upper abdominal pain. The pain had persisted for five hours and was accompanied by prolonged vomiting. Examination revealed him to be in definite shock, with cold and clammy skin, moderate cyanosis and a rapid and thready pulse. The patient cooperated very poorly with the examination and was often incoherent. The abdomen was severely tender in the epigastrium and left upper quadrant where there was moderate spasm. Liver dullness was present and the lower abdomen showed no spasm or tenderness. Immediate infusion was started and transfusion ordered. Meanwhile a flat plate and an upright film showed no free air under the diaphragm or evidence of intestinal obstruction. A Levin tube was placed in the stomach and continuous Wangensteen suction instituted. Antibiotics, sedation and oxygen were also ordered. Within the next several hours there was a gradual recovery from shock.

An electrocardiogram showed no abnormalities. Subsequent serum amylase showed 390 mg. per 100 cc. and the white blood count was 12,800 with 92 per cent neutrophils. During the next 24 hours there was a mild recurrence of shock with a return of severe epigastric pain. A transfusion was given at this time and a second serum amylase showed 368 mg. per 100 cc. During the following 48 hours the patient improved gradually and was able to tolerate a soft diet after removal of the Levin tube. Although abdominal tenderness persisted, the patient said he felt well and was determined to leave the hospital, which he did on the following day.*

Comment and Conclusions

The majority of these patients, treated medically with success, had much the same acute onset of abdominal pain and shocklike symptoms as those who subsequently were brought to surgery. However, in contradistinction to those in the surgical group, they had in common *an early, obvious, favorable response to treatment* with moderate sedation, gastric suction, large doses of antibiotics and parenteral fluids.

It cannot be proved that all of these patients were suffering from acute pancreatitis, but such was the considered opinion of the attending internists and consulting surgeons even in those patients whose serum amylase tests fell within normal limits. In addition, it is noted that in this group there was: (1) an average serum amylase of 509 mg. per 100 cc.; (2) an average white blood cell count of 13,711 with 84 per cent neutrophils; and (3) pancreatic tenderness persisting for some time after the earlier resolution of abdominal pain. It must also be noted that in most of these patients an etiologic agent was present capable of initiating the pancreatic inflammation. For example, in case 1, trauma; case 2, mumps; case 3, alcoholism; case 6, chronic cholecystitis and pancreatic calculi.

The ultimate prognosis in this group is interesting in that each of the patients (except in cases 1 and 2 where trauma and parotitis were the exciting agents) may have a common biliary-pancreatic channel favoring the recurrence of the acute illness. Consideration must be given to the possibility of recurrent attacks which might indicate sphincterotomy, as advocated by Doubilet and Mulholland.[2]

Acute pancreatitis is a markedly variable disease which must be approached with an open mind as regards its treatment. Like most disease processes, it may be so mild that treatment is incidental to its spontaneous resolution or it may be severe enough to thwart the most vigorous therapy. Rigid adherence to preconceived notions of management in the face of laboratory-weighted diagnosis may bring about unnecessary complications and even fatal results.

The cases that continue to make up the mortality figures of acute pancreatitis are: (1) those in which necrosis and hemorrhage are so severe and shock so overwhelming and rapid that death seems inevitable despite any form of treatment;[21] and (2) those in which moderate necrosis and hemorrhage result in shock which, although temporarily well combated by modern methods, becomes gradually irreversible as lack of specific relieving meas-

*Six additional cases treated medically, being of a similar type, have been omitted because of space limitations. The additional case reports will appear in full in the author's reprints. The cases treated medically described here are illustrative of the others.

ures allows the galloping enzymatic process to continue. It is this second group with which this paper is concerned.

Much of the controversy regarding the proper treatment of acute pancreatitis has arisen from previous "statistically" poor results with surgery at a time when preoperative, operative and postoperative supports were either nonexistent or not sufficiently developed. It is recognized that it is desirable to drain the abdomen surgically of the ferments, debris and blood produced by acute pancreatitis and to nullify, if possible, the exciting cause of the disease. But surgeons fear the shock of the disease—the shock which the same surgeons enthusiastically treat with transfusions, stimulation, oxygen, modern anesthesia and rapid surgical correction in such conditions as penetrating abdominal trauma, perforated peptic ulcer, acute intestinal obstruction, mesenteric embolus, ruptured ectopic pregnancy, etc.

I do not doubt that there are many cases of "responding pancreatitis" where a course of watchful waiting should be maintained, but I wish to point out that in recent years the emphasis on the medical treatment of acute pancreatitis has been too adamant, based on too barren academic data. In this regard it is enlightening to read the views favoring surgical intervention from the writings of Rhoads, Howard and Moss,[21] Raker and Bartlett,[22] Fine[23] and Ogilvie.[24]

From the factors considered, it seems prudent to consider each case of acute pancreatitis as one which, in its early stages, contains the possibilities of self-limitation and resolution, but which also contains the inherent potential of self-perpetuation to the point of death of the patient from shock, toxemia and exsanguination. Pancreatitis is an illness, therefore, which must be observed and treated in much the same way as, for example, bleeding peptic ulcer. That is, follow the patient intimately by clinical means and observe each minute sign of response to treatment as recorded by the blood pressure, blood count and accessory laboratory aids, but more importantly by the return of a normal pulse, the arrest, relief or retrogression of shock and intestinal or cardiorespiratory complications, and the evident and definite subjective overall improvement of the patient. Throughout the period of medical observation, surgical preparations must be made simultaneously so that the attempt can be made, if need be, to interrupt the headlong enzymatic rush, which can result in the death of the patient.

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The Ideal Tonsillectomy

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WHEN one contemplates the list of complications of adenotonsillectomy, he usually feels an immediate challenge to devise a technic that will abolish all of these unfavorable occurrences. It is the purpose of this report to outline some of the major contributions which have helped prevent the complications of adenotonsillectomy.

Avoiding Primary Hemorrhage

After reviewing the literature and putting the many suggestions to a practical test, I have concluded that the closed-fossa tonsillectomy devised by Emerson[1] is the most effective method for eliminating immediate post-tonsillectomy hemorrhage. In suturing the fossa closed without including the pillars, the suturing usually is begun at the lower pole. The sutures must enter where the tonsillar pillar joins the true floor of the fossa. The needle is inserted near the posterior pillar, passed under the true floor of the fossa, and brought out as near the junction of the anterior pillar and fossa as possible. Interrupted sutures, figure-of-eight sutures, or a continuous suture may be used. The floor of the fossa should be tented up with a clamp to allow the most room possible between the floor of the fossa and the structures beneath. Emerson[2] recently has devised a plastic flap for closure of the fossa.

Primary adenoid bleeding may be avoided by performing the adenoidectomy first and by packing the nasopharynx tightly. After the tonsils have been removed, the surgeon may remove the adenoid packs.

Avoiding Secondary Hemorrhage

A great deal has been written about this complication, and many suggestions have been made to prevent it. The deleterious effect of acetylsalicylic acid has been pointed out by

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Jones[3] and other authors and the beneficial effects of vitamins C and K have been demonstrated by Coombs[4] and many authors. The use of antibiotics to avoid infection has been stressed as another important factor in preventing postoperative bleeding.

However, the surgical technic which most nearly approaches the ideal one is that of Emerson.[1,2] When this technic is used, late bleeding does not occur, since the wound heals by primary intention and the bed of granulations from which hemorrhages arise does not form. Of course, this does not prevent secondary adenoid bleeding, but this has been rare and mild in my experience.

Avoiding Psychic Trauma

Coleman[5] has listed seven principles of management that are of vital importance in avoiding the psychologic sequelae that sometimes follow adenotonsillectomy. These principles are as follows: (1) The child should be given a calm and honest explanation of the need for the operation; (2) he must be spared the tension and anxiety reflected by the attitude of the parents; (3) in order to avoid surprise and confusion, the hospital, operating room and nurses should be explained to the child; (4) the reason for the anesthesia also should be explained; (5) the presence of one or both parents should be permitted during the induction of anesthesia and in the postanesthetic period; (6) if the fifth suggestion is impossible, the separation of the child from the parents will be made easier if the surgeon will accompany the child to the operating room; (7) the child should be permitted to manifest his hostility during the postoperative period.

Many stories with illustrations now are available for explaining the need for the operation and for introducing the child to all of the participants. The play drama described by Bach[6] is an excellent means of preparing a child for such an experience.

Barhash[7] recently has written an excellent critique on the psychic trauma that may result from tonsillectomy in cases in which the patients are children. His objections to afternoon operation, which requires that the child must wait anxiously for many hours with an empty stomach and in a strange environment, are well taken. His suggestions for avoiding psychic trauma do not differ from those of Coleman.[5] Premedication is the most important factor in the prevention of this complication. This will be considered more fully with the description of the anesthetic technic.

Avoiding Infected Remnants of Tonsils and Adenoids

A common complication of adenotonsillectomy is the presence of residual tags of infected lymphoid tissue, although it is seldom listed as such. In order to prevent this complication, Hyde[9] has recommended that the use of devices such as tonsillotomes and snares be abandoned and that the tonsils be removed completely by sharp dissection from superior pole to inferior pole. In my experience, this procedure has been most effective in eliminating this complication. Hyde[9] also stressed the many advantages of the Crowe-Davis mouth gag and the Rose position, which permit the surgeon to sit at the head of the patient.

Avoiding Bulbar Poliomyelitis

If one grants that bulbar poliomyelitis is sometimes a complication of adenotonsillectomy (and it certainly seems that it is),[10] one cannot escape the rational principle of avoiding this operation during those months when the incidence of the disease is abnormally high. Whether prophylactic inoculations will eventually prevent this complication remains to be seen.

Avoiding the Complications of General Anesthesia

Anesthesia for adenotonsillectomy continues to stimulate more discussion and occupy more pages in the medical literature than does the technic for the operation.[11] This is, of course, as it should be, since most of the tragic complications of this operation are due to the anesthesia.

What are the requirements of the ideal tonsillectomy anesthesia? Belton and Leigh[12] state that it must be the safest and the least unpleasant, and that it should allow the proper working conditions for the surgeon. To ac-

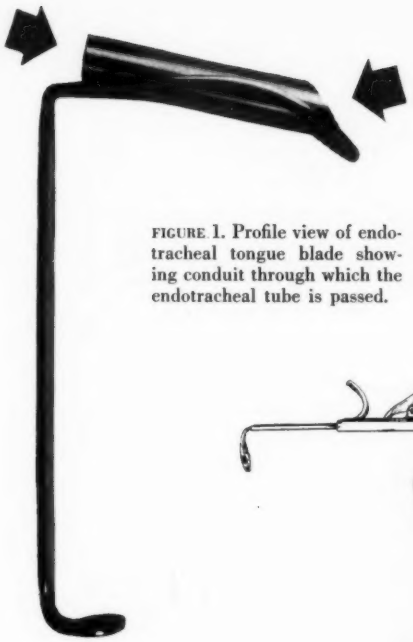

FIGURE 1. Profile view of endotracheal tongue blade showing conduit through which the endotracheal tube is passed.

complish this, many surgeons have recently described technics which include the use of the Crowe-Davis mouth gag, the Rose position, and the intravenous administration of thiopental sodium. The largest series of cases in which these technics have been employed have been reported by Hayes,[13] Blaisdell,[14] Griffiths[15] and Johnson.[16] However, an endotracheal tube was not employed routinely in the series of cases reported by these authors. Most anesthesiologists agree that this is a nec-

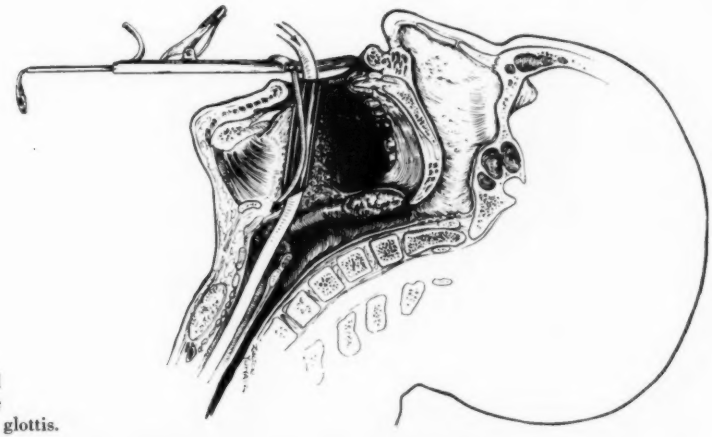

FIGURE 2. Endotracheal tube passing through the tongue blade and into the glottis.

FIGURE 3. Endotracheal tongue blade in a McIvor mouth gag with the endotracheal tube attached to the anesthetic source. The handle of the tongue blade is resting on a Mayo stand, and the instruments are immediately before the surgeon.

FIGURE 4. Anesthesiologist aspirating the tracheobronchial tree after tonsillectomy.

essary adjunct for the safe use of thiopental sodium as an anesthetic for oropharyngeal operations.[17,18]

The need, therefore, for an anesthetic technic which could be used for children and adults and which would prevent aspiration, hypoxia and laryngospasm was the challenge that led to the development of the endotracheal tongue blade.[19] I have used this device in a series of cases in which adenotonsillectomy was performed on children and adults, and it appears to be effective in preventing these complications and their secondary sequelae, such as lung abscess, cardiac arrest, cerebral injury[20] and death.

The instrument is a tongue blade of three sizes designed to fit either the Crowe-Davis or the McIvor mouth gag, but so constructed that a conduit is included in the tongue depressor portion through which an endotracheal tube passes (figure 1). The patient is anesthetized, and an endotracheal tube passed. Thereafter, the mouth gag, with the endotracheal tongue blade attached, is inserted into the mouth, while the endotracheal tube is allowed to slide through the conduit. It sometimes is necessary to grasp the endotracheal tube with a tonsil hemostat and pull the rubber tube through the stainless steel conduit tube. Figure 2 shows the endotracheal tube in place extending from the connection with the anesthetic source through the tongue blade conduit and down into the trachea. Figure 3 shows the instrument and operating room setup with the shank of the tongue depressor attached to the Mayo stand across the patient's chest. This provides easy access to the surgical instruments and avoids the assistant's tiresome task of holding the mouth gag upright.

Surgeons finally have a device which allows endotracheal intubation without interfering with the surgical field in any type of oropharyngeal operation. Because the endotracheal tube is inserted into the tongue blade, it protrudes into the oral cavity only slightly and it is held firmly to avoid its slipping out of the glottis or from side to side in the mouth.

It is apparent that with this new technic the anesthesiologist is free to use any medication or anesthetic agent that he desires. No longer is he limited to certain agents that are "the only safe ones to use for operations on the throat" (no matter how unpleasant for the patient). The premedication can be heavier, and psychic trauma thus can be minimized.[21]

PENTOTHAL® sodium may be administered rectally to produce basal anesthesia. General anesthesia can be induced more pleasantly by the intravenous administration of an agent such as Pentothal sodium, SYNCURINE® or SURITAL® sodium. Cyclopropane or nitrous oxide may be used. When these agents are used, consciousness is regained more rapidly than with intravenously induced anesthesia.

After the surgeon has completed the operation, the anesthesiologist may aspirate the tracheobronchial tree with a catheter (figure 4) through the endotracheal tube, and the hypopharynx may be aspirated again. The mouth gag, endotracheal tongue blade and endotracheal tube are removed in unison.

This technic overcomes all the objections that have been raised against the use of Pentothal sodium without intubation. The patient awakens when the endotracheal tube is withdrawn, and the entire respiratory tract has been cleansed of all secretions. The technic permits the maintenance of an adequate airway throughout the operative procedure.

Hayes[13] was one of the first surgeons to use Pentothal sodium as the sole anesthetic agent for tonsillectomy. He experienced some difficulty in maintaining an adequate airway in 2 of the 82 consecutive cases in which this anesthetic agent was used, and postoperative laryngospasm occurred in 6 cases. Slater and Stephen[18] have said that the use of an endotracheal tube will tend to eliminate these complications. With the development of the endotracheal tongue blade, the final objections of surgeons to the use of Pentothal sodium anesthesia have been overcome. The endotracheal tube does not interfere with the operative field, and it does not have to be shifted from one side to the other in order to permit the surgeon to remove each tonsil.

Summary

An ideal technic for performing adenotonsillectomy includes the use of the closed-fossa

tonsillectomy devised by Emerson,[1] the dissection recommended by Hyde,[9] and the endotracheal tongue blade described by Barton.[19] I have used this technic in more than 100 cases in which tonsillectomy has been performed on adults and children. Not a single complication has occurred in any of these cases. The technic has had the hearty endorsement of the anesthesiologists, who for years have found that it is most difficult to produce anesthesia safely for this operation.

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Postgraduate Clinical NOTES

26. LEUKAEMIA

The leukaemic process must be regarded as, in the broadest sense, neoplastic; it is a cellular proliferation, apparently purposeless, without evident cause, and ultimately irreversible. It differs from most other tumours in being multicentric or systematized, but in a biological sense it is as malignant as any other neoplasm. . . .

In human leukaemia the aetiological importance of only one factor is established, and this is radiant energy. The disease is eight times more common in radiologists than in other members of the medical profession, and the Japanese have reported its incidence in survivors of the atomic-bomb explosion at Hiroshima to be eight times that of the general population of Japan.

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Differential Diagnosis of Diffuse Pulmonary Infiltrations

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ALTHOUGH it is comparatively easy to establish the presence of diffuse pulmonary infiltrations by roentgenograms, to determine the underlying cause may be difficult.

In addition to roentgenograms, a careful medical history and physical examination of patients with diffuse pulmonary infiltration should be obtained. Extensive laboratory studies, blood cultures, sputum examination, and biopsy of bone marrow and peripheral lymph nodes may be necessary to reach a correct diagnosis. The value of such skin tests as the tuberculin, histoplasmin, coccidioidin, toxoplasmin and blastomycin tests cannot be overemphasized.

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Bronchoscopy may reveal a bronchogenic carcinoma from which there are extensive metastases throughout the lungs. This procedure also serves as an excellent means to obtain fresh specimens of bronchial secretions. A pulmonary biopsy may also be absolutely necessary to establish the diagnosis. The technic of pulmonary biopsy makes available an adequate specimen of lung tissue for pathologic, bacteriologic and chemical analyses.

Conditions capable of producing diffuse pulmonary infiltration are certainly numerous. At first the problem of differential diagnosis may appear difficult and complex, but with careful analysis and the many tests available, it should be possible to arrive at a correct diagnosis.

If proper therapy and a reliable prognosis are to be given it is imperative that the causative factor or factors of diffuse pulmonary infiltrations be correctly established.

JOHN B. ANDOSCA

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Pulmonary Tuberculosis

In the great majority of cases the diagnosis of pulmonary tuberculosis is not difficult, but there are few diseases in which a careful history is so essential. The family history as well as the patient's past history are important. No two patients present the same history or symptoms. The usual symptoms are cough, expectoration, loss of appetite and weight, weakness and night sweats. Two symptoms which must be investigated are hemoptysis and attacks of idiopathic pleurisy, especially pleurisy with effusion. Although the physical examination sometimes reveals very little, it often shows persistent rales in the upper third of the lung. Pulmonary tuberculosis can be diagnosed earlier and with more certainty roentgenographically than by any other single method.

FIGURE 1. Roentgenogram in a case of pulmonary tuberculosis showing patchy type of infiltration, especially marked in the upper lung fields, and small cavities in both apexes. The patient was a 35 year old white man who had a six week history of cough, expectoration, weakness, dyspnea and loss of appetite and 26 lb. Sputum positive for tubercle bacilli. Patient is now on antimicrobic therapy and doing well.

It is important to examine the sputum for tubercle bacilli; if the sputum is negative, gastric and culture tests are indicated. Sometimes the tuberculin test may be very helpful in making a diagnosis. (Figure 1.)

Miliary Tuberculosis

Miliary tuberculosis is considered under the general heading of hematogenic tuberculosis since the disease is spread by a sudden invasion of the blood stream by tubercle bacilli. Often the primary tuberculous lesion is not recognized and the onset of miliary tuberculosis may be insidious. The illness is characterized by a gradually increasing pulse rate and pyrexia, headache, malaise, drowsiness and weakness. The pyrexia may be continuous, remittent or inverted. Examination of the chest may reveal remarkably few abnormal signs. The patient rapidly becomes more ill. The spleen may be palpable.

Three diagnostic procedures of considerable value are liver biopsy, bone marrow biopsy and ophthalmoscopic inspection of the retina for choroidal tubercles.

Miliary tuberculosis may cause no roentgen changes for as long as three or four weeks after the onset of symptoms. The lesions are visualized as small, uniform, millet-seed-sized nodules scattered diffusely throughout both lungs. Occasionally the lesions of the upper lobes appear somewhat larger than those in the lower lobes. Rapid bronchopneumonic spread of pulmonary tuberculosis resembling miliary tuberculosis has been observed in some cases of profuse hemoptysis. (Figures 2 and 3.)

Chemical Pneumonitis

Pulmonary involvement becomes evident within a few hours after the aspiration and/or ingestion of such chemicals as kerosene, fur-

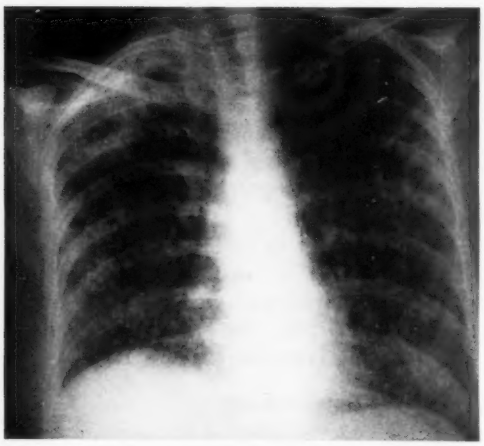


FIGURE 2. Roentgenogram in a case of miliary tuberculosis showing fine miliary and nodular infiltration throughout both lungs. There is an underlying chronic tuberculous process in the right apical region. The patient was a 28 year old white woman who had a two week history of cough, headache, weakness and pyrexia. Despite intensive antimicrobic therapy, she died; the diagnosis was confirmed at autopsy.

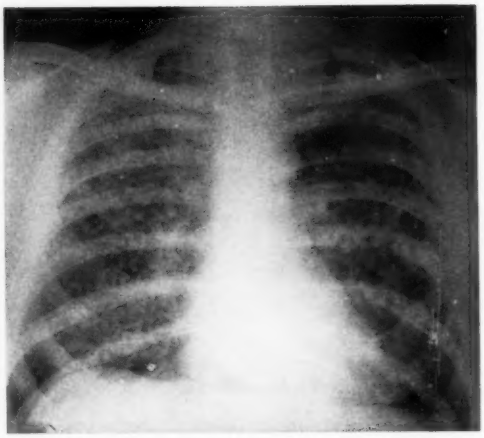


FIGURE 3. Roentgenogram showing bronchogenic spread of pulmonary tuberculosis. A bilateral miliarylike infiltration was accentuated in the right upper lobe, site of the chronic tuberculous process. The spread followed persistent hemoptysis. The patient was a 42 year old white man who had a three week history of cough, expectoration, loss of appetite and weight, and hemoptysis. Two years before he had had a right-sided tuberculous pleural effusion.

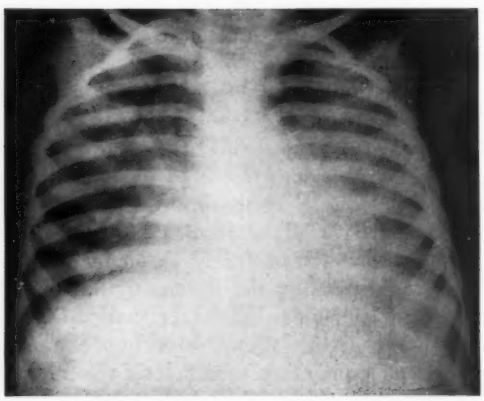


FIGURE 4. Roentgenogram in a case of chemical pneumonitis. Note the fine clouding and ground-glass appearance of the parenchyma extending from hilar shadows, predominantly in the middle and lower lung fields. The patient was a two year old white boy who had ingested some furniture polish and whose symptoms were coughing and some vomiting. He responded well to antibiotic therapy and was discharged after three weeks of hospitalization.

niture polish, turpentine and cleaning fluid. The main symptoms are usually respiratory. The patient complains of cough, gagging or strangling. Vomiting, lethargy, drowsiness, stupor or convulsions may occur, depending on the amount of the chemical absorbed. Roentgenograms should be taken as soon as possible to determine the extent of pulmonary involvement.

Pneumonitis is the most frequent finding, but emphysema, pneumothorax, pleurisy, pneumonia and pleural effusion may appear. Roentgenologic changes precede clinical manifestations and are often marked in the absence of physical findings.

In mild cases, patchy consolidation is observed in the cardiophrenic angles. In more severe cases, diffuse opaque consolidation extends from both hilar areas to the periphery of both lung fields; this consolidation later resolves into fine, mottled densities. Treatment is aimed at the rapid, thorough removal of the ingested irritant from the gastrointestinal tract. (Figure 4.)

Periarteritis Nodosa

Periarteritis nodosa is a widespread polyarteritis affecting chiefly the smaller and medium-sized arteries. It is believed to be a postinfectious disease or due to a filtrable virus. Inflammation and necrotic changes affect the adventitia, the media and, finally, the intima of the smaller arteries of the various organs. With involvement of the intima, thrombosis and infarction occur. In the initial stages all the symptoms of an acute infection appear, with pyrexia, prostration, sweating and rapid loss of weight. There is usually an eosinophilia. Signs of acute cardiac or renal failure may develop. In other cases acute pulmonary, cerebral or renal infarction or hemorhage may result. The diagnosis is extremely difficult unless a biopsy of a subcutaneous node is done. The prognosis is very poor. (Figure 5a.)

Bronchopneumonia

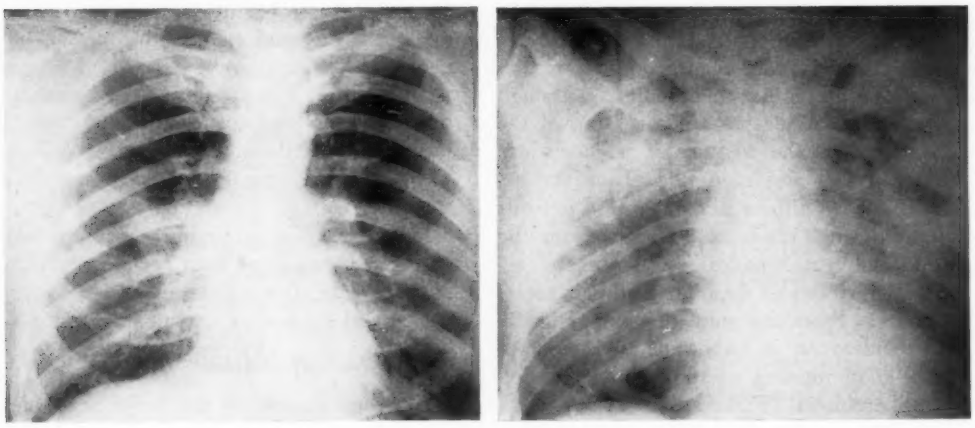
Bronchopneumonia is an inflammation of the terminal bronchioles and air vesicles, involving part or all of the lobule. In most cases, the inflammatory process occurs in patchy or confluent areas usually scattered throughout both lungs, with maximum involvement usually occurring at the bases. Although at least half of these cases are caused by the pneumococcus, other bacteria may be involved, and the infection is frequently mixed. The disease may develop as a complication of measles, whooping cough, sinusitis or tonsillitis. The aspiration variety results from inhalation of septic material. The inhalation of irritant gases or vapors may produce a very extensive bronchopneumonia.

The patient usually complains of a productive cough, occasionally blood-streaked sputum, dyspnea, varying degrees of cyanosis and restlessness. The temperature is often remittent with hyperpyrexia. The diagnosis of bronchopneumonia usually presents few difficulties when it develops in the course of one of the infectious diseases such as measles. The early recognition of the causative agent is very important so that proper therapy may be instituted. (Figure 5b.)

Pneumoconiosis

The principal inorganic dusts which injure the lungs contain silica. Silicosis occurs in

FIGURE 5. Roentgenograms of a 46 year old white man with a two month history of pyrexia, weakness, joint and abdominal pains, hematuria and hemoptysis. His blood picture showed the presence of anemia and eosinophilia of 18 per cent. a *(left)*. Admission chest film showing periarteritis nodosa with moderate thickening and prominence of the hilar shadows. Triangular area of probable atelectasis extending out from the right hilus may simulate a pulmonary tumor. b *(right)*. Chest film one month later showing diffuse bronchopneumonia with irregular areas of consolidation in both lung fields. These areas have hazy borders and tend to coalesce. The diagnosis of periarteritis nodosa was made at autopsy one month after hospital admission.



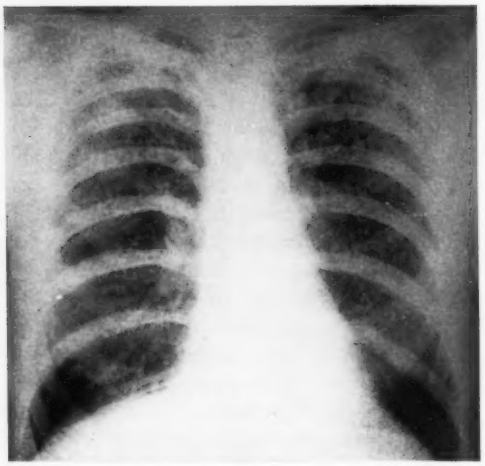


FIGURE 6. Roentgenogram in a case of silicosis showing diffuse nodular infiltration more pronounced in the upper and middle lung fields with some compensatory emphysema in the bases. The patient was a 52 year old white man, a coal miner for 28 years, who had a history of cough, slight expectoration and dyspnea. The sputum was persistently negative for tubercle bacilli.

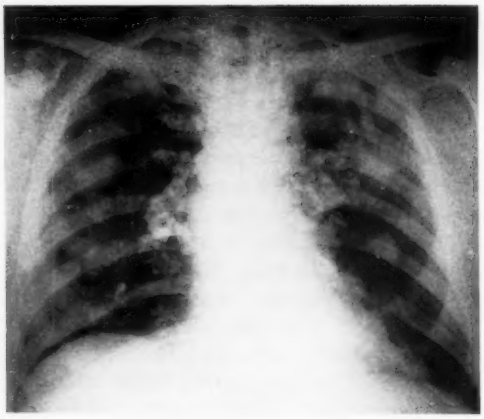


FIGURE 7. Roentgenogram in a case of silicosis demonstrating the so-called egg-shell calcified nodes in the hila and areas of consolidation in the upper lung fields. Consolidation is usually seen in the more advanced stages of the disease. The patient was a 61 year old white man, a granite cutter for 34 years, who had a history of cough, expectoration, weakness and dyspnea. The sputum was negative for tubercle bacilli.

workers in cement and ceramic industries, in those mining silicic materials, in sandblasters and in those engaged in manufacturing some abrasive soaps. A history of exposure and roentgenograms of the chest usually suffice to make a diagnosis. The pneumoconioses are all characterized by a progressive general fibrosis of the lungs, causing dyspnea of varying severity with cough and expectoration. A common variety is the so-called peribronchial perivascular lymph node type. In the other common variety, the roentgenogram resembles that seen in miliary tuberculosis, although larger confluent masses are seen toward the hilus. Grossly, the nodules in silicosis are firm, spherical and indurated. They are accompanied by diffuse fibrosis which extends radially through the lung tissue, involving the mediastinal lymph nodes. The so-called egg-shell calcification of the hilar glands is sometimes seen. From the point of view of industrial accidents it is important to remember that a good number of these cases develop silicotuberculosis. (Figures 6 and 7.)

Pulmonary Carcinosis

The clinical manifestations of pulmonary carcinosis often present a difficult diagnostic problem. Symptoms referable to the primary neoplasm are frequently absent or are masked by the pulmonary symptoms. The most striking and constant findings are cough, occasional streaking, progressive dyspnea, chest pain, cyanosis, low-grade fever, weight loss and weakness. Physical examination of the lungs may disclose relatively few signs, usually medium rales. The appearance and configuration of the pulmonary lesions offer little aid in determining the site of the primary lesion. The site of the primary neoplasm may be the stomach, rectum, prostate, breast or genitourinary tract. The origin of the primary lesion will remain unsolved in a certain percentage of cases even after a thorough clinical investigation and exhaustive necropsy. (Figure 8.)

Fungous Infestation

Fungous disease of the lungs presents no

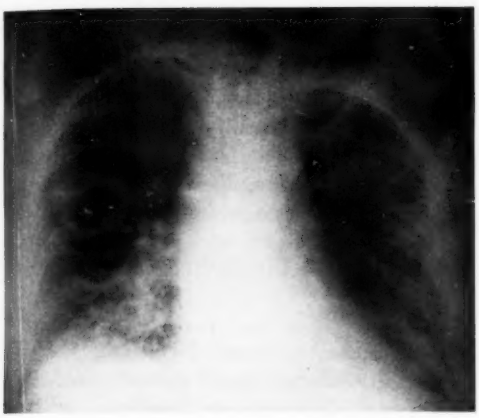


FIGURE 8. Roentgenogram in a case of lymphangitis carcinosis showing areas of fairly discrete infiltration ranging from ½ to 3 cm. in size and scattered throughout both lung fields, especially marked at the right base. The patient was a 77 year old white woman who had a six month history of loss of appetite and 28 lb. Two months later she complained of cough and some pleuritic pain. The diagnosis of carcinoma of the colon with metastasis to the lungs was confirmed at autopsy.

distinctive clinical picture and may simulate a number of well-known pulmonary conditions, particularly moniliasis, blastomycosis, coccidioidomycosis, actinomycosis and aspergillosis.

The clinical symptoms of fungous disease vary in degree and type depending on the virulence of the infection and on how widely and rapidly it spreads. In mild cases the symptoms are those of cough, occasional chest pain and loss of strength. In severe cases the patient may complain of a severe cough, expectoration, dyspnea, hemoptysis and fever.

Physical examination of the lungs often fails to reveal any abnormal findings, although in some cases there may be physical signs of dullness, rales and cavitation. The radiologist's interpretation of the roentgenograms is very important. The characteristic radiologic feature of such infections is the tendency to widespread infiltrations, abscess formation and involvement of the mediastinal lymph nodes. Diffuse large nodules, extensive densities, cavitation and miliarylike spread may be seen.

The diagnosis can be confirmed by demonstrating the fungus itself and by positive skin tests. Most fungous infections of the lungs respond quite favorably to iodide, sulfonamide, penicillin and vaccine therapy.

Moniliasis

Bronchopulmonary moniliasis is an infection of the lungs caused by the *Candida albicans* and characterized by a chronic and usually progressive course.

Candida (formerly named *Monilia*), which is widely distributed in nature, is a genus comprising a number of species and possible

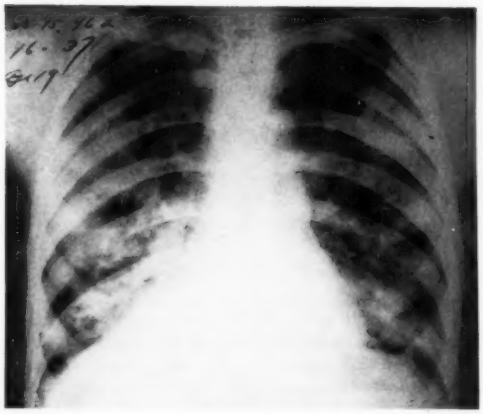


FIGURE 9. Roentgenogram in a case of fungous infestation showing bronchopulmonary infiltration of *Candida* involving both middle and lower lung fields. Note the small pseudocavity shadows in the areas of consolidation, especially at the bases. The patient was a 19 year old white man, a grocery clerk, who had a six week history of cough, expectoration, fever and dyspnea. The diagnosis was confirmed by culture examinations of the sputum and by autopsy.

varieties. The organism exists as a saprophyte, but is believed to become parasitic under certain conditions. The yeastlike fungus can be cultured on Sabouraud's medium and is diagnostic of this condition. (Figure 9.)

Blastomycosis

The diagnosis of blastomycosis usually is made by finding the characteristic organisms in the sputum and by positive skin tests. In

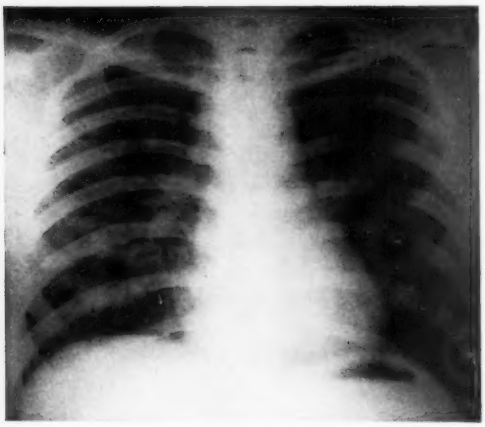
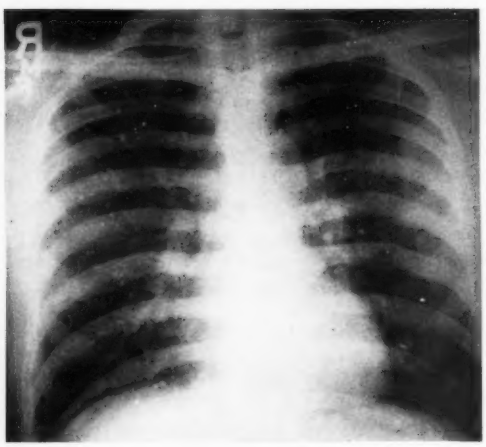


FIGURE 10. Roentgenogram in a case of blastomycosis showing the more localized infiltrative process in the right middle and lower lung fields. The infiltration in these cases is not characteristic and cannot be readily differentiated from nonspecific pneumonitis or atypical tuberculosis. The patient was a 21 year old white man who had been rejected for military service. The diagnosis was confirmed by culture and skin tests. He responded to iodide therapy and is now in good health.

FIGURE 11. Roentgenogram in a case of histoplasmosis showing calcified nodes, which are usually small (½ cm. or less) in size, scattered in the parenchyma of both lungs and in the hila. The calcifications are not localized in one lung area, as is usually the case in an arrested primary complex. The patient was a 21 year old Negro man who had been rejected for military service and was asymptomatic. The histoplasmin test was positive, 1:1000, and the tuberculin test was negative. He is alive and well 11 years after the diagnosis.

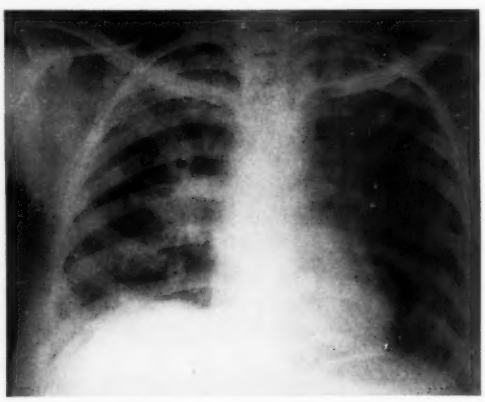


most cases there may be blastomycotic lesions of the skin in addition to the pulmonary involvement. The actual presence of the organisms in the blood has been demonstrated. Systemic cases are usually fatal, the patient dying with the clinical picture of tuberculosis. Subacute and chronic miliary lesions are common in blastomycosis, although the nodules are said to be coarser and less sharp than miliary tubercles. (Figure 10.)

Histoplasmosis

Histoplasmosis is caused by a fungus, *Histoplasma capsulatum*. It is characterized by hepatomegaly, splenomegaly, general or regional enlargement of the lymph nodes, protracted fever, emaciation, secondary anemia and leukopenia. Not infrequently symptomless individuals are found, on roentgen examination, to have multiple small calcific densities scattered rather uniformly throughout both lungs. They vary in size, number and distribution. Enlarged hilar lymph nodes, accentuated bronchovascular markings and pleural thickening may be present. The diagnosis can be made with the histoplasmin skin test, or by demonstrating the causative fungus by

FIGURE 12. Roentgenogram in a case of sarcoidosis showing irregularly outlined enlargement of the hilar shadows with diffuse nodular parenchymal infiltration extending laterally from the hila. There are a few areas of sarcoidal consolidation in the upper lung fields. The patient was a 30 year old Negro woman whose lung disease was discovered on routine chest x-ray. The diagnosis was confirmed by biopsy of a cervical node. The patient is alive and well eight years after the diagnosis was made.



staining smears of peripheral blood or bone marrow specimens. (Figure 11.)

Sarcoidosis

Sarcoidosis is a disease of unknown etiology. Many competent investigators using precise methods of study have failed to clarify the etiology and, in particular, the relationship to tuberculosis. Granulomatous lesions resembling tubercles without caseation develop in the regional and mediastinal lymph nodes, spleen, bones and skin. The disease as a rule follows a slow, benign course with spontaneous healing. More rarely, a fatal course is observed with involvement of the lungs, nervous system and heart. Lymphadenopathy and splenomegaly are usually present. Occasionally the uveal tract of the eye and the parotid glands are involved. No specific therapy is known although we have seen several cases improve markedly with streptomycin. (Figure 12.)

Hodgkin's Disease

Typically, Hodgkin's disease begins in the cervical lymph nodes and involves in order the axillary, inguinal, mediastinal and retroperitoneal nodes. The disease tends to spread to the entire reticuloendothelial system and may metastasize widely. Usually, young adults are affected but the disease occurs at all ages. The blood studies show a steadily progressive anemia of the secondary type. It is said that the eosinophils increase in number as the disease progresses. The fever may be of the Pel-Ebstein type. In typical Hodgkin's disease the tissue, in addition to its cellular lymphoid character, contains binuclear giant cells (Sternberg-Reed cells) and numerous eosinophils and the fibrotic stroma of the node increases. The clinical course usually terminates fatally in from three to five years. (Figure 13.)

Löffler's Syndrome

Löffler's syndrome is usually characterized by transitory pulmonary infiltrations, a benign course and eosinophilia. This disease has become much more important because of the difficulty in differentiating it from other pulmonary diseases, especially tuberculosis and

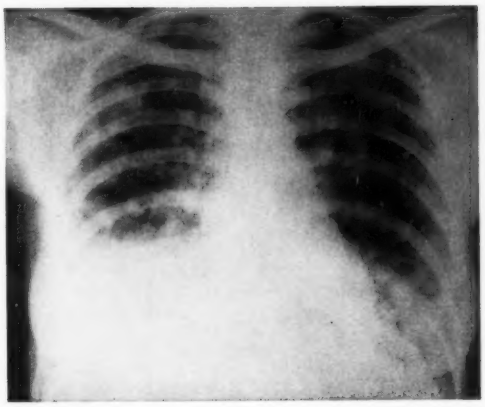


FIGURE 13. Roentgenogram in a case of Hodgkin's disease showing pulmonary manifestations of a generalized body involvement. There are somewhat rounded, large and small areas of infiltration in both lungs with no gross lobular adenopathy in the hila. There is a small amount of fluid at the right base. The patient was a 28 year old white woman who had a nine month history of swollen glands of the neck, cough and weakness. Examination revealed enlarged cervical and axillary glands, liver and spleen. Diagnosis was confirmed by biopsy of a cervical node and at autopsy three months later.

malignancy. The cause of the condition is not clearly defined. Some describe it as a syndrome having an allergic etiology, with asthma and other hypersensitivities.

Some cases may be completely asymptomatic. Many patients complain of cough, slight expectoration, loss of appetite and weight, fatigue, fever, shortness of breath and substernal pains.

The blood picture is extremely important. The percentage of eosinophils may reach as high as 65 per cent. Sputum examinations may also reveal the presence of eosinophils. The roentgen findings are characterized by the presence of irregular, fleeting areas of infiltration or mottled densities in almost any portion of the lungs.

The treatment of this condition is by either blood transfusions or cortisone. The prognosis is very good. (Figure 14.)

Cystic Disease of the Lungs

The etiology of cystic disease of the lungs is not entirely clear. The condition may be

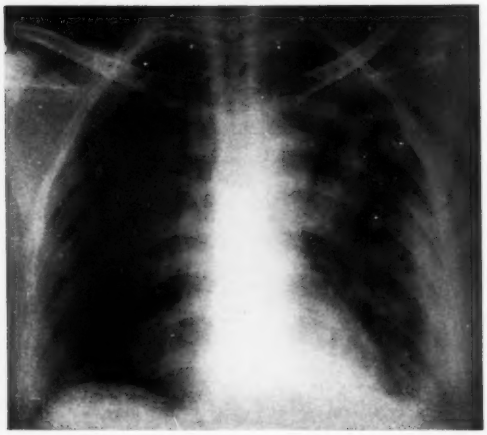


FIGURE 14. Roentgenogram in a case of Löffler's syndrome showing a bronchopneumonic type of infiltration scattered throughout most of the left lung. Roentgenograms are not diagnostic. The diagnosis was confirmed by laboratory findings. The patient was a 27 year old white woman who had a three week history of coughing. Blood study showed an eosinophilia of 35 per cent. She recovered completely with cortisone therapy.

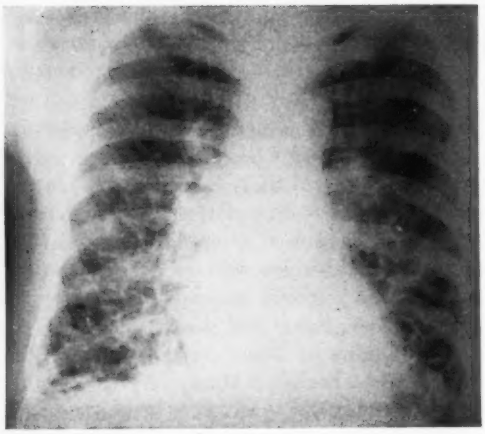
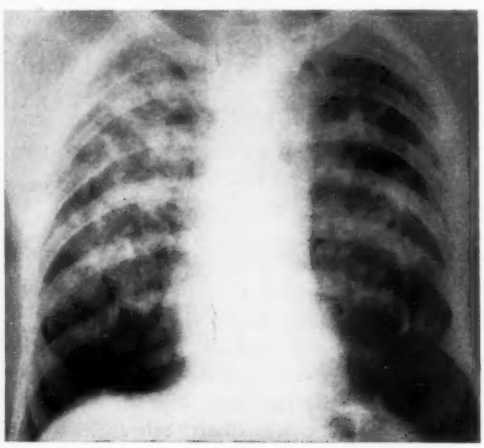


FIGURE 15. Roentgenogram in a case of polycystic disease showing thin-walled radiant shadows about 1 to 2 cm. in size occupying a good portion of both middle and lower lung fields. There was no parenchymal reaction noted about the walls of the cysts. Some of the cysts at the right base contain a small amount of fluid. The patient was a white man who had a three month history of cough, expectoration, weakness and dyspnea on exertion. He is alive and fairly well eight years after the diagnosis was made.

either congenital or acquired. Some cysts of the lungs are the sequela of an inflammatory process and others are entirely noninflammatory. They may be either bronchial or parenchymal in origin, single or multiple, and they may contain fluid or air or both. If lung cysts become infected they may present all the findings characteristic of pulmonary suppuration. Some solitary cysts may reach an enormous size. Cases have been reported in which such a cyst has replaced an entire lung. The large cysts are characterized by displacement of the heart and mediastinum to the opposite side with dyspnea as the prominent symptom. The cysts are usually sharply defined, with no surrounding area of pneumonitis such as is often seen in tuberculosis cavities. The honeycomb or polycystic variety involves both lungs and is quite rare. It occurs in younger patients, usually men, and often produces secondary effects on the lungs and heart (cor pulmonale) with subsequent death.

In the diagnosis of cystic disease of the lungs the roentgenologic examination is by far the most important procedure. Ordinary

FIGURE 16. Roentgenogram in a case of pulmonary granulomatosis showing ground-glass clouding and parenchymal density in both lung fields. There are superimposed linear dense shadows with longitudinal axes in both lungs. These shadows in the apexes may simulate fibroid tuberculosis. The patient was a 37 year old white man, a furniture repairer, who had a two month history of cough, progressive dyspnea, loss of weight and weakness. All sputum and skin tests were negative. The diagnosis of pulmonary granulomatosis was established by pulmonary biopsy. Autopsy performed two years later confirmed the diagnosis.



anteroposterior and lateral views should be used, although bronchography is also of value in some cases. (Figure 15.)

Pulmonary Granulomatosis

Pulmonary granulomatosis is characterized by an irritative cough, occasional chills and fever, moderate weight loss and exertional dyspnea. Clinical examination of these patients usually reveals variable degrees of respiratory distress even at rest, depending on the amount of pulmonary involvement. Cyanosis and clubbing of the fingers may be present. Chest expansion is often limited and the vital capacity is reduced. Chest roentgenograms characteristically show diffuse nodular shadows, and as the disease progresses the lung fields acquire a ground-glass haziness. The right auricle and the pulmonary conus are prominent in extensive cases. The course is usually progressive and eventually death results from right heart failure. (Figure 16.)

Summary

1. Roentgen manifestations of diffuse pulmonary infiltrations vary widely.

2. The cause of such lesions may present a difficult diagnostic problem.

3. In addition to a thorough physical examination, it is essential to obtain a careful history, roentgenograms and fluoroscopic studies, skin and sputum tests and laboratory studies. Bronchoscopy and gland and marrow or pulmonary biopsy should be performed if indicated.

4. It is not possible to institute proper therapy and give a reliable prognosis unless the causative factor of diffuse pulmonary infiltrations is determined.

5. Clinical, laboratory and roentgenologic aids in the diagnosis of 16 cases of diffuse pulmonary infiltration have been discussed.

Postgraduate Clinical NOTES

27. REHABILITATING THE AGEING POPULATION

Experience of old people both before and after the inception of the National Health Service led [him] to say without hesitation that the provision of suitable spectacles was far and away the most important single thing that could be done to maintain the useful activity of old people. Alleviation by hearing-aids of the decline in hearing that so often accompanied old age probably came next to spectacles in importance. The argument for the provision of these aids to perception became all the stronger when it was remembered that cerebral mechanisms in old age required a greater sensory input than in youth, and that this was the very period when the special peripheral receptors themselves became so liable to structural defects. A further means of sustaining the vigour of the old lay in attention to their feet. This presented a major challenge to preventive medicine. Finally, the key to physical vigour in many old people lay in their mental state. Nothing sapped physical strength more surely than the mental torpor that followed a loss of interest in life.

J. H. Sheldon, *British Medical Journal*, July 31, 1954, p. 297

Cataract: Essentials for the Non-ophthalmologist

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ALTHOUGH it is the ophthalmologist who is necessarily concerned with the more esoteric aspects of cataract, certain essentials concerning this subject should also be familiar to all physicians.

WILLIAM CHARLES CACCAMISE

Definition

Unfortunately, to laymen and even to some physicians, the word "cataract" immediately implies grave ocular disturbance. In reality, cataract means any opacity, no matter how minute, of the lens of the eye. Consequently, cataract and visual loss are not necessarily one and the same. Whether a cataract is to be accompanied by a disturbance in vision depends on the size, position and density of the opacity. Opacities located in the periphery of the crystalline lens and behind the iris do not intercept any of the light rays that normally reach the retina, and therefore do not interfere with vision. Opacities located axially, and particularly posteriorly, intercept a portion of the more important light rays that normally enter into the formation of the retinal image and consequently are more likely to reduce visual acuity.

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Anatomy

Understanding of cataract is predicated on a knowledge of the anatomy of the normal eye lens. The lens is a biconvex, transparent structure which lies behind the iris, forming a backdrop for the pupil. The central points of its surfaces are termed the anterior and posterior poles, and the line joining these the axis of the lens. The crystalline lens consists of (1) a hyaline capsule which surrounds the lens completely and whose anterior and posterior components meet at the margin or equator of the lens, (2) epithelial cells that lie immediately beneath the anterior capsule and extend only to the equator, and (3) the lens substance proper, which in children and ado-

lescents is completely pultaceous, but in adults consists of an outer pultaceous cortex and a firmer central nucleus.

Pathology

In general, cataractous changes consist of degeneration of the lens fibers, either sclerosis or necrosis, associated with some aberrant activity of the epithelium.[1] Diminished metabolism, decreased capsular permeability, and loss of substances active in oxidation (glutathione and vitamin C) are important biochemical features.[2]

Incidence

Almost everyone has some degree of opacity of the crystalline lens. Peripheral punctate and dustlike opacities are usually already present in infancy.[3] Most of these minute opacities, however, are visible only by examination of the lens with a biomicroscope (combination of slit lamp and corneal microscope). More definite changes are evident, particularly in the inferior nasal periphery of the lens, in the eyes of more than 50 per cent of persons past 60 years of age.

Diagnosis

Diagnosis of cataract naturally depends on the finding of an opacity within the eye lens. With the following procedure, most gross lens opacities can be demonstrated:

1. *Dilatation of the pupil*—Adequate evaluation of the crystalline lens ideally requires a pupillary diameter of at least 6 mm. The safest noncycloplegic mydriatics (drugs that dilate the pupil without paralyzing the ciliary muscle) are PAREDRINE® hydrobromide 1 per cent and a solution consisting of NEOSYNEPHRINE® hydrochloride 5 per cent and EUPHTHALMINE® hydrochloride 5 per cent. Adequate dilatation usually can be obtained in 30 to 45 minutes with the use of either of these solutions in patients who have blue eyes. The Neosynephrine-Euphthalmine solution is more effective in those with brown eyes. The use of mydriatic drugs is contraindicated in cases of narrow-angle glaucoma. In any case in which there is a shallow anterior chamber or a history of glaucoma or suggestive of glaucoma, dilatation of the pupil should be the responsibility of the qualified ophthalmologist.

After the pupil has been dilated and the lens and fundus have been examined, a miotic (a drug that constricts the pupil) must be instilled. The patient is requested to remain in the office until the pupil has returned to normal size. Two drops of pilocarpine hydrochloride 2 to 4 per cent or eserine salicylate 0.25 per cent are usually adequate. Atropine, homatropine and scopolamine (hyoscine) should not be used except by an ophthalmologist, for these drugs produce not only prolonged dilatation of the pupil (with a greater possibility of precipitating an attack of acute congestive glaucoma in a patient with an unrecognized narrow anterior chamber) but also paralysis of the ciliary muscle (cycloplegia) which will inconvenience the patient, particularly for close work, for one to several days.

2. *Ophthalmoscopic examination of the pupillary reflex*—The pupillary reflex as seen through the ophthalmoscope with a zero lens in the viewing aperture is normally a homogeneous orange-red. To obtain this reflex, the observer should view the pupil from a distance of approximately 12 inches. If there are opacities in the cornea, lens or vitreous body, the homogeneity of the reflex will be disturbed—black flecks, black stripes or a black network will be seen within the orange-red area. By having the patient look up or down and by observing the resultant direction of displacement of the opacity, one can determine whether the opacity is in the cornea or anterior half of the lens or in the posterior half of the lens or the vitreous body. If the opacity is displaced in the same direction as the eye has moved, it is in the cornea or anterior half of the lens. If it moves in the opposite direction, the opacity is in the posterior half of the lens or the vitreous body. Furthermore, if an opacity which has been localized to the posterior half of the lens or the vitreous body is not in a fixed position, it must lie in the vitreous body. A central ring reflex which moves only slightly with the movement of the eye suggests a nuclear cataract.

Some physicians find the pocket flashlight more suited to examination of the pupillary

reflex than the ophthalmoscope. Direct illumination with the pocket flashlight usually enables the examining physician to determine whether an opacity is located in the cornea or in the crystalline lens. The light beam is first directed onto the cornea in a search for opacities. An opacity will appear as a grayish haze or whitish spot, depending on its density, in a normally transparent cornea. Certain corneal opacities may be more evident in one particular position of the eye. Therefore, the patient is instructed to look up, down, right and left. After the cornea has been examined carefully, the light should be directed into the dilated pupil. Because the lens normally reflects a certain amount of light, the normal pupillary reflex obtained with the pocket flashlight will not be a jet black, but a grayish black. Lens opacities which are large enough to be seen without the aid of magnification will appear as grayish-white areas in the more normal grayish-black. A central yellowish to brown haze indicates nuclear sclerosis or, if sufficiently dense, a nuclear cataract.

The examining physician may be confused by obtaining a completely black pupillary reflex with the ophthalmoscope. This most commonly results when one who uses the ophthalmoscope infrequently attempts to elicit the reflex through a miotic pupil. Dilatation of the pupil will usually reveal a normal orange-red reflex in these cases. When the reflex is actually black even after dilatation of the pupil, the explanation usually lies in the presence of a very dense corneal opacity, an advanced cataract or, most likely, a massive vitreous hemorrhage. Collaborative use of the ophthalmoscope and the pocket flashlight will frequently reveal the exact cause.

Management of Suspected Cataract

When the general practitioner suspects that cataractous changes are present in one of his patients, the patient should be managed as follows:

1. Refer the patient to a competent ophthalmologist for a definite diagnosis and classification of the opacities. In many cases the ophthalmologist, through use of the ophthalmoscope, the pocket flashlight and especially the slit lamp, can determine whether the opacities are obviously progressive or stationary and whether they are significant or insignificant. He may also be able to advise the family physician concerning specific conditions that should be looked for in a general physical examination.

2. Obtain a thorough history and perform a general physical examination to rule out a possible etiologic factor.

Treatment

The only practicable procedure to restore vision in a case of diminished visual acuity due to cataract is surgical removal of the cataract. Medical treatment is not effective for primary lenticular opacities not associated with systemic or ocular disease. In cases of secondary cataract, treatment of the associated systemic or ocular disease only rarely prevents progression of the cataract and even more rarely results in regression. DIONIN® or fish-lens extract is of no value, and the latter is actually potentially dangerous.

Indications for Surgery

Surgical procedure is indicated when the neuroretinal system of the concerned eye is apparently intact but the cataract has reduced the visual acuity to a point inadequate for the patient's purposes. If immature cataracts are present bilaterally or in one eye and the visual acuity with both eyes open is sufficient for the patient's purposes, surgery is not indicated. Extraction of the cataract from one eye in such a case will require the patient to decide after the operation which eye he will use. He cannot use both eyes simultaneously unless both eyes have been operated on, because the operated eye will require a very thick lens in front of it if the patient is to see well with that eye. Such a corrected operated eye will have a retinal image 25 per cent larger than that of the unoperated eye. The brain cannot fuse two images that are so different in size. Double vision (diplopia) or suppression of one eye will result. Although a few very competent ophthalmologists enthusiastically recommend the use of a contact lens for the operated eye in an attempt to obtain binocular vision in

such cases, this is generally not practicable.

A possible indication for removing a cataract when the vision in the other eye is adequate is the presence of a mature or hypermature cataract. Such a cataract may be a potential danger to the survival of the involved eye, and some authorities believe its extraction is advisable even though vision in the other eye may be perfect. The patient will continue to use only the normal unoperated eye, but the operated eye can be considered to be in reserve, should vision ever be lost in the unoperated eye.

Contraindications to Surgery

The mere presence of cataractous changes does not make surgery mandatory. In fact, if any of the following conditions are present, surgery is contraindicated:

1. Vision which is adequate for the purposes of the patient, with neither eye containing a mature cataract.

2. Evidence that in spite of a successful removal of the cataract, vision in the operated eye will not improve.

The following prognostic tests are routinely carried out by the ophthalmologist to determine whether or not the perceptive system which is hidden by the lens opacities is apparently intact:

Light perception and projection—In spite of the cataractous changes, the patient should be able to perceive a point source of light and also locate it accurately.

Colors—In spite of the cataractous changes, the patient should be able to identify colored light. Blue, red and green usually are utilized in this test.

Pupillary reaction—In spite of the densest cataract, the pupil should respond normally to light.

A poor response to any one of these prognostic tests suggests a defect in the perceptive system behind the cataract. The prognosis for recovery of good vision after surgery would therefore be extremely guarded.

In addition, whenever possible, the fundus should be evaluated ophthalmoscopically. Visualization of the optic disk and macula is extremely important. In most cases of cataract in which surgical removal would be indicated, the fundus cannot be adequately inspected. However, if the patient has been followed for some time prior to surgery, adequate visualization of the fundus usually has been possible at some time. In some cases of nuclear cataract that are ready for surgery the fundus can still be seen fairly well.

3. A patient for whom a surgical procedure would be contraindicated generally, or who has a very limited life expectancy.

Surgical Procedures Used

Although it is unnecessary for the general practitioner to have any profound knowledge of the surgery of cataract, the following information may be of some interest and value in obtaining an over-all understanding of the subject. In general, the selection of operation depends on the age of the patient. Formerly, adults with cataracts were not subjected to surgery until a condition known as "ripe cataract" had been attained. The operative procedure of choice was the so-called extracapsular cataract extraction, in which the surgeon breaks the anterior capsule of the lens and attempts to express the lens material contained within the capsule. A "ripe cataract" is a mature cataract, one in which the entire lens contents have become cataractous. When the lens capsule has been torn away, the entire lens contents can be easily expressed—somewhat analogous to expressing a pea from a pod. If the cataract is not ripe, i.e., if part of the cortex is not cataractous, it is very difficult to express this noncataractous material. The cortex is sticky and tends to adhere to the remaining lens capsule. This complicates the postoperative course, and a second operation, i.e., needling, is frequently required because an after-cataract forms (primarily a conglomeration of lens capsule and cortex that remains to obstruct the pupil).

Modern American cataract surgery emphasizes the intracapsular extraction of the cataract, i.e., removal of the cataractous lens *in toto*. The surgeon makes every attempt not to open the capsule of the lens. Therefore, the term "ripe cataract" has lost much of its significance in modern cataract surgery. Fortu-

nately, the intracapsular method is now being used in the United States. Previously a patient often had to wait years for his cataract to become mature or "ripe" before he could have surgery, in spite of the fact that he was already greatly incapacitated by reduced vision. It is important that the patient be eligible for surgery as soon as his vision is no longer adequate for his purposes. With the one exception previously discussed, the cataract's effect on the patient's vision, not the maturity of the cataract, should be the criterion for surgery. The intracapsular operation permits application of this basic principle.

For very young children a method known as needling of the cataract is carried out. The lens capsule is opened with a knife needle, in the hope that exposure of the lens to the aqueous humor will cause the lenticular contents to be dissolved. This method is feasible in children because there is no firm nucleus in a child's eye lens. Needling is not performed as a primary procedure on the adult eye because the lens contains a nucleus which could not be dissolved by the aqueous.

Ophthalmologists may differ as to whether an extracapsular or an intracapsular extraction should be performed in cases of patients between the ages of 25 and 40 years. In general, the younger the patient the more resistant the zonular attachments of the lens. An attempt to extract a cataract intracapsularly in spite of undue zonular resistance may result in serious surgical difficulties. For this reason, many ophthalmologists routinely perform an extracapsular extraction in cases of adults less than 40 years of age.

In examining the eyes of patients who have undergone cataract surgery, the general practitioner may have noticed a keyhole defect in the pupils of some, while in others the pupils appeared normal. The reason for this is that there are three methods of handling the iris during any surgery performed for cataract:

1. The iris is left completely intact. This method is usually reserved to needling or linear extraction in children.

2. A complete iridectomy is performed. A portion of the iris at 12 o'clock is excised, so that the pupil has a keyhole configuration.

3. A peripheral iridectomy is performed. A small opening is made in the iris, usually at 12 o'clock, but the pupil retains its normal shape. Iridectomy is done to discourage postoperative prolapse of the iris.

Prognosis for Restoration of Vision

According to Kirby,[4] the prognosis for restoration of vision following removal of uncomplicated cataract is excellent; 85 to 90 per cent of the patients achieve good useful vision. In the remainder of the cases, complications modify the result so that less than useful vision or no vision is achieved.

Summary

Although the exact diagnosis and specific treatment of cataract are the responsibility of the ophthalmologist, the general practitioner should have an understanding of certain essentials concerning this common ocular condition. This article presents such essentials. The role of the general practitioner in such cases is to suspect cataract, direct the patient to a competent ophthalmologist for an exact diagnosis, and collaborate with him by ruling out systemic disease and determining whether it is safe from a general point of view for the patient to be subjected to surgery.

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CASE REPORT

Rehabilitation in the Older Age Group

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THE problems of the aged have been stressed repeatedly by prominent leaders both in medicine and in government. All too often, the attitude toward the aged and supposedly infirm person is that "if taking care of him at home becomes too much of a problem, it may be necessary to put him in a nursing home." If this attitude persists, within the coming 20 to 30 years the permanent inhabitants of our hospitals and nursing homes will be our aged population. The population trends and the advances in medical science with the resultant increase in longevity make this a certainty. The aged should not be relegated to the scrap pile so readily, nor should our hospitals be utilized for a dumping ground for the aged.

However, medical science has also made definitive advances in the field of medical rehabilitation. The concept stressed by Dr. Howard A. Rusk, that of treating the total individual with a view toward his living a full life to the limits of his abilities, has broadened the horizon for the aged—the largest segment of our population.

An example of what can be done for a patient who receives the living death sentence, "Put him in a nursing home," follows:

A 69 year old railroad conductor had a cerebrovascular accident in August 1950, with a resultant right hemiplegia and slurring of speech. Recovery was sufficient for him to return to work, although incoordination of movements persisted. In December 1950 a "virus" infection developed, and he was hospitalized for a few weeks. He then noticed difficulty in walking and coordination. His condition improved gradually until September 1953, when progressive deterioration in coordination and in his ability to walk began, as well as an increasingly severe mental depression. By December 1953, the patient could take only one or two steps without assistance and had great difficulty in initiating walking. He fell repeatedly and showed a growing fear of any attempt to walk. Normally cheerful and

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of bright disposition, he completely lost interest in things going on around him, and his voice became reduced to an inaudible whisper.

He was referred to a competent neurologist, who reported: "He takes small, shuffling steps, which interfere with his getting about. Every once in a while he is able to take almost normal steps. He has some weakness of the right lower facial muscle innervations. He is over-reactive emotionally—at times depressed, then stubborn—and shows other evidences of deterioration in that he cannot subtract 7 from 100. His speech is somewhat slurred and there are times when his concentration is defective. His blood pressure is 170/108, and there is an aortic systolic murmur. I have no doubt that we are dealing with the diffuse effects of cerebral arteriosclerosis, as you correctly surmised. Considering his age, 69, I am not hopeful that much can be done. Apparently insomnia is a stubborn problem and for it I would suggest use of DORMISON® in 250 mg. or 500 mg. capsules. It might also be advisable to give him intramuscular injections of nicotinic acid in flush dosage (10 to 20 or 30 mg. once or twice a week) and during the day a DEXAMYL® tablet on arising and half a tablet early in the afternoon. If taking care of him at home becomes too much of a problem, it may be necessary to put him in a nursing home at some future time."

Physical examination at the Institute of Physical Medicine and Rehabilitation showed a depressed elderly man whose speech was slurred and almost inaudible. Blood pressure was 165/110, RSR, PR = VR, EH, harsh systolic murmurs at base and apex. AS, MI, A2 > P2. Classification II-III, B-C. Classification was difficult because of the patient's limited physical activity. He was able to stand without assistance but most attempts to walk resulted only in a shuffling of the feet without any forward movement. When a few weak steps were taken, he dragged his right foot and his trunk was overbalanced forward. Approach to furniture, doorways and people halted his progress. Muscle tests disclosed moderate generalized weakness of the trunk and lower extremities. The only abnormal neurologic findings were a positive Romberg sign and a right facial paresis. He was found to be self-sufficient in his activities of daily living insofar as self-care and dressing activities were concerned. His major problem was one of ambulation activities.

Psychologic testing revealed that the patient fluctuated in his emotional adjustment and when pushed too hard would slip back. This, however, is to be expected with organic brain damage.

The patient was started on a program of coordination exercises, ambulation training and occupational and speech therapy. We found that a shock reaction (i.e., clapping hands) and reciprocal arm-foot gait pattern sometimes helped to start him walking. For a month, treatment was given twice weekly for half a day and was coordinated with a home program of exercises. During this time, the patient's depression lifted moderately but he improved only slightly in his ability to walk. On muscle testing, however, the left hip and trunk musculature improved from P (+) to G, and the right hip, knee and trunk from P and F (+) to F and G.

He was also given BENADRYL® (50 mg. four times daily) together with his exercises, and shortly afterward there was rapid improvement physically and emotionally. He was soon able to start walking with almost no hesitation, and his endurance rapidly increased. With speech therapy, volume control became more steady and intense. His desire and ability to initiate conversation increased and soon became apparent in everyday communication. Those treating him noticed that he smiled and talked voluntarily in a clearer voice. His family also noticed a change; once again he took an interest in things about him and entered spontaneously into family conversations, but they felt that this was the outcome of the improvement generally. He also was able to get around the house unassisted and without falling, thus reducing greatly the amount of care necessary. The treatment program was then progressively reduced and in a short time the patient was discharged on a home maintenance program, no longer a burden to the family, with renewed vigor and interest in "the remaining years of his life."

SCIENTIFIC EXHIBIT

CONSERVATIVE MANAGEMENT OF DIABETIC FOOT COMPLICATIONS

W. L. LOWRIE,[1] W. EARL REDFERN[2] AND BROCK E. BRUSH[3]

HENRY FORD HOSPITAL, DETROIT, MICHIGAN

[1]Physician-in-Charge, Division of Metabolism; [2]Associate, Division of Metabolism; [3]Senior Associate, Division of General Surgery, Henry Ford Hospital, Detroit, Michigan.

Adapted from an exhibit shown at the 1954 Annual Meeting of the American Medical Association, San Francisco, California.

Foot Hygiene of the Diabetic

Most Lesions Are Preventable

CONTROL DIABETES

To resist infection
To combat hyperlipemia, atherosclerosis and neuritis

FOOT HYGIENE

Bathe feet daily, avoiding excessive soap to preserve natural oil
Keep skin soft with oil or lanolin

SOCKS

Two sizes or one-half inch longer than feet to avoid binding the toes together

SHOES

One-half inch space beyond great toe
Wide, to permit toe movement and ventilation
Army last—great toe straight
Smooth lining
Change shoes daily
Wear new shoes one hour at a time for breaking-in
Avoid shoe nails
Do not walk barefoot

EFFECTS OF SHOES

AVOID FOOT INJURIES AND INFECTIONS

Trim nails straight across, not too short, with corner outside nail fold
No hot water (or chemical) bottles or electric pads
Avoid strong antiseptics
No corn plasters or paring of corns
    Relieve pressure; soften; trim as corn protrudes
Prevent or treat calluses
    Remove pressure; soften. Callus leads to ulcer and cellulitis

Short shoes

Ill-fitting shoes

Walking barefoot

Ill-fitting artificial leg

EFFECTS OF SHOES

Ill-fitting artificial leg

New shoes worn all day

Electric pad burn

Improper nail trimming

Ingrown nail

Gangrene from hot water bottle

Foot Injuries and Infections

FOOT INJURIES AND INFECTIONS *(Continued)*

Cellulitis from infected callus

Callus treated by lanolin; initial appearance

After one month

After six months

Handling Foot Complications of the Diabetic...

EVALUATION

- Walking capacity, degree of symptoms
- Careful clinical examination
  - Palpation of vessel walls and pulses
  - Condition of skin and subcutaneous tissues
  - Relative color and warmth
- Results of conservative regimen
- Other available tests
  - Occlusion index
  - Sympathetic blocks
  - Arteriography

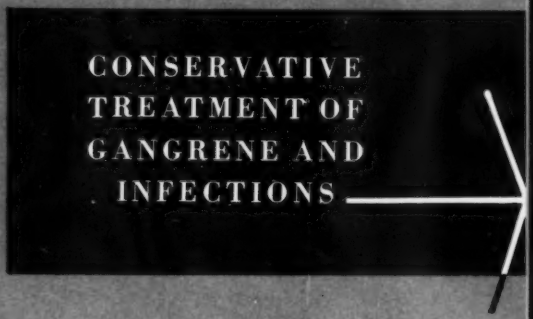
MANAGEMENT

- Diabetic control
- General health
- Protection against physical and chemical injury
- Antibiotics
- Vasodilators
- Anticoagulants
- Consider sympathectomy

CONSERVATIVE SURGICAL PRINCIPLES

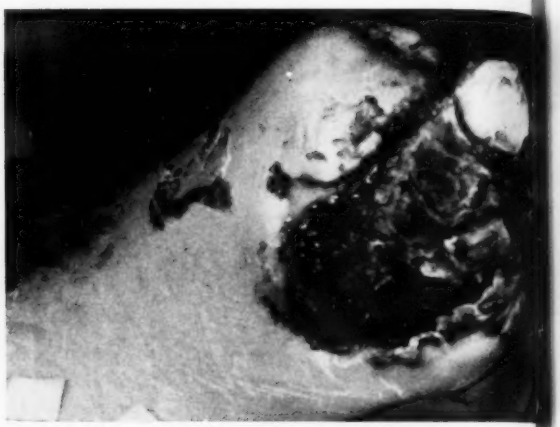
- Adequate incisions for infection
- Antibiotics
- Trial of conservative management
- Débridement
- Local amputation
- No tourniquet or tight dressing

CONSERVATIVE TREATMENT OF GANGRENE AND INFECTIONS



GANGRENE

H. M., 75 years old. Progressive arterial occlusion affecting one toe after another for 10 years. No surgery.



One month extension into foot

◀Extension into foot

One year; heads of metatarsals drop off with toes

Two years; complete healing

GANGRENE

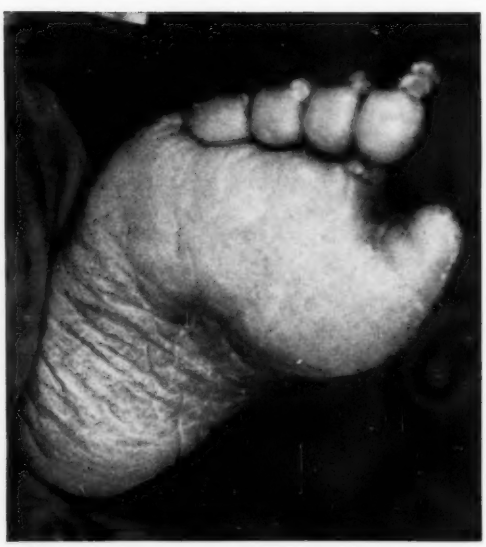
N. B., 58 years old. Dropped hammer on toe. All extremities pulseless. Auricular fibrillation. Heart failure.

Thin, tight, atrophic skin

GANGRENE

Two months; tip of toe dropped off in four months

Five months; healed. No antibiotics



Wide incision

Two weeks; extensive sloughing

INFECTION

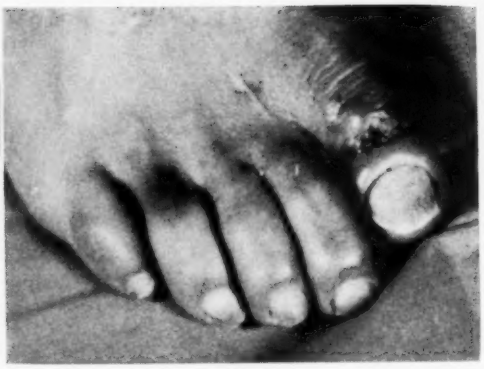
B. K., 59 years old. Injured foot on cement block, causing infection of deep plantar tissues. Amputation had been advised.

Three and one-half months; skin graft

Four and one-half months; functioning foot

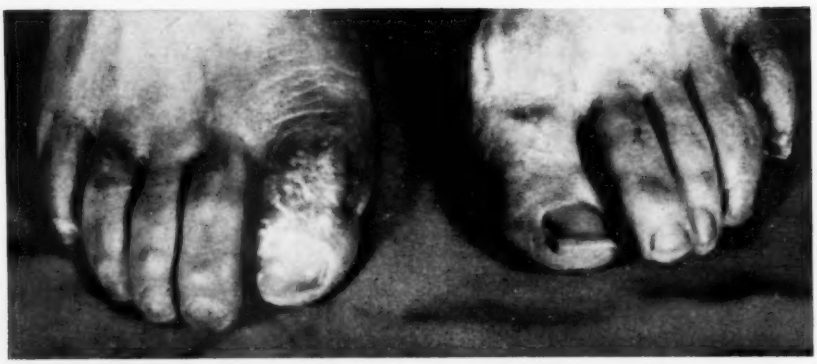
OSTEOMYELITIS

T. M., 52 years old. Infection of fascia and bone after cutting off a callus. Circulation poor.



Eight months; hot soaks

Fourteen months; bone of middle phalanx extruded



Healed; toe functions without middle phalanx

GANGRENE and INFECTION

F. B., 64 years old. Right leg amputated five years previously. Ulcerated callus on left great toe. Circulation fair. Job depended on saving leg.

One week; dry gangrene

Two weeks; gangrenous tissue removed

Six weeks; infection of tendons and bone, head of metatarsal extruded

Eleven months; healing. Patient has worked for one year

Urology in Childhood

JAMES A. HARRIS AND SAMUEL A. VEST*

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PEDIATRIC urology is not a distinct field or specialty, but simply the application of modern diagnostic and therapeutic methods in genitourinary disorders of childhood. Until recently this aspect of urology was somewhat neglected because of certain technical obstacles and a laxity of professional interest.

A newborn infant today can safely receive a complete urologic examination with the same exact methods employed in an adult by the use of the modern miniature cystoscopes which allow accurate observation and delicate endoscopic manipulation. Another great advance is the more general use of excretory urography, with which unsuspected urinary tract disease in children is now commonly demonstrated.

Of equal value is the professional education at all levels to the importance of urologic disease in children. The general profession should recognize the incidence and the clinical manifestations of the many insidious urologic conditions which occur in childhood, and the serious renal damage which results. Many of these disorders lead to unnecessarily premature termination of life, and many deaths occur in early childhood because of disease which could and should have been recognized and corrected.

JAMES A. HARRIS

SAMUEL A. VEST

Meredith Campbell[1] states that one-half of all children have some form of urologic disturbance before they reach puberty. Alertness on the part of pediatricians and family physicians whenever a child has symptoms referable to the urinary tract, followed by proper detection and management, will unquestionably save and prolong life.

It is often said that a child is a small adult

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and as such is subject to the same diseases. Except for pyelitis of pregnancy and hyperplasia or cancer of the prostate, the genitourinary tract of a child may be affected by all the specific disease processes found in an adult. However, the manifestation of these processes differs markedly, and in treating children who have urologic disease the urologist must share the pediatrician's appreciation of the greater nutritional needs, the increased tendency to dehydration and electrolyte disturbances, the high susceptibility to infection, and the known variations in reactions to anesthesia, including anoxia. For example, it must be appreciated that disease of the urinary tract is very common in the young, but equally important is the fact that little or no correlation may exist between the symptoms and the severity of the underlying disease. It is not rare to see a child whose outward appearance is that of robust health but who has unilateral renal destruction; even more disturbing, it is not unusual to find profound disease of the urinary tract in the presence of a normal urinalysis.

This article is not intended to be encyclopedic in scope, but rather to call attention to and discuss briefly the more important pathologic states that occur in childhood and to outline the urologic procedures indicated.

Urinary Tract Infection

Infection in the urinary tract is the most common and most easily recognized urologic disease. In children it has its greatest incidence in the first several years of life. It is said to outrank all bacterial disease in children less than two years of age and to account for 3 to 4 per cent of all problems in general pediatric practice. Urologists who have studied the subject in detail conclude that most cases of urinary tract infection pass unrecognized in young children, with only the virulent or resistant cases attracting clinical attention. This disorder is commonly thought to be a complication of infection located elsewhere, especially in the respiratory and intestinal tracts; in the latter it is frequently a sequela of diarrhea.

The incidence of urinary tract infection is particularly high in female children; in most such cases it is thought to be a urethrocystitis with or without secondary ascending renal infection. When manifestations of the latter occur, too many physicians assume that the infection is a simple pyelitis, but it has been established that pyelitis, as such, never occurs. Any inflammation of the renal pelvis or calyces always involves the renal cortex (pyelonephritis) to a variable degree, resulting in some renal destruction. The greater incidence of urinary tract infection in female children probably can be explained on the basis of the shorter urethra whose distal end may harbor colon bacilli. From this area, infection may spread by either direct continuity, the lymphatics or the blood stream to the interior of the urinary system.

Any infection that becomes established in the urinary tract, by whatever route, is increased in its severity and chronicity by the presence of congenital abnormalities, especially those which cause stasis or obstruction of the urinary stream. Most urologists believe that urinary tract infection will eventually develop in 50 per cent of all cases of anomaly and stasis. As a corollary, studies of chronic infection in the urinary tract disclose that in three out of four cases an associated underlying factor is present and that this factor frequently is an anomaly. Also, the incidence of chronic infection in children who have anomalies of the urinary tract is 20 times that in children who do not have such anomalies. Campbell found in one series of 1,102 children with chronic pyuria that 307, or 27 per cent, had anomalies of the ureter or pelvis of the kidney.

On the other hand, cases of urinary tract infection are discovered in which there is no evidence of associated underlying disease such as anomaly, stasis, foci of infection, or bowel disorder. Such simple uncomplicated infections in which bacteria gain access to the urinary tract usually are self-limited and will disappear clinically irrespective of the treatment employed.

Most infections in the urinary tract in childhood are caused by the common organisms found in such infections in adults—*Escher-*

ichia coli, Aerobacter, Pseudomonas aeruginosa (pyocyaneus), the enterococci and occasionally the staphylococci and streptococci. Most infections, and especially those of the chronic type, are due to the gram-negative bacilli found in the intestinal tract in which there may be one or more of these organisms in combination with enterococci.

For diagnosis in the case of a male child, urine should be collected in two glasses, after the meatus has been cleansed, and the specimen in the second glass examined. In the case of a female child it is important to wash the vulva thoroughly and obtain a specimen from the urinary stream while the vulva is spread. If this is not practical, a catheterized specimen is necessary, because a simple voided specimen in the female often includes leukocytes which originate not from the urinary tract but from the urethral meatus and the vestibule.

Ideal treatment in cases of urinary tract infection begins with a urine culture to identify the precise causative organism. It may be advisable to determine the in vitro response (sensitivity test) of the cultured organisms to the currently available chemotherapeutic agents. This procedure, however, adds to the expense and is impractical in many practices. Therefore, treatment in most cases can begin without precise identification of the infecting organism, providing certain precautions are exercised. A careful history will help one to determine whether the infection is initial, chronic or recurrent. If one concludes that the infection is recurrent or chronic, the likelihood of an underlying anatomic disorder is great and a prompt, complete urologic survey is in order. If the infection is an initial one, with no prior symptoms (unexplained fever, pain in the flank, enuresis, frequency or burning on urination, etc.), acceptable treatment consists of one or possibly two courses of treatment with the modern antibiotics. These in general have been GANTRISIN®, THIOSULFIL®, various combinations of the multiple sulfonamide compounds, and antibiotics of the tetracycline series, such as TERRAMYCIN® and AUREOMYCIN®.

If the infection does not disappear promptly, within one or two weeks, or if it recurs, a thorough urologic survey is indicated. This survey includes appraisal of the upper urinary tract by either intravenous or retrograde pyelography.

Disorders of other systems involving the gastrointestinal tract and on rare occasions the nasopharynx have been known to result in repeated infections in the urinary tract. Consideration therefore must be given to these systems as well as to the urinary tract in cases of recurrent or chronic urinary tract infection.

Most simple infections (without underlying disorders) will respond to therapy with the modern antibiotics. Adjuvant measures may include proper fluid intake, good anal hygiene, and correction of chronic constipation. With regard to the latter, ingestion of cultures of the acidophilic bacilli and drugs to alter the flora of the gastrointestinal tract sometimes leads to complete disappearance of urinary tract infection.

Complicating factors such as hydronephrosis, calculi, ureterocele or reduplication of the kidneys require surgical correction to relieve stasis and remove diseased tissue before the infection can be completely eradicated. Urologists frequently find severe underlying disease and extensive infection only after months of medical or chemotherapeutic treatment directed against what seems to be a resistant or frequently recurring urinary tract infection. The consequence of delay in diagnosis and logical management may be extremely detrimental to the future welfare or even to the life of the patient.

Congenital Anomalies

It is not generally appreciated that 35 to 40 per cent of all maldevelopments in the human body occur in the genitourinary system. Many of these anomalies result in early death. Autopsy figures alone indicate at least 12,000 deaths a year among children with such malformations. If the deaths in cases in which the diagnosis is not established were included, the figure would be considerably higher. Genitourinary malformations are about the sixth most common cause of death in young children.

Most major anomalies in the urinary tract cause some degree of urinary obstruction or stasis, so that anomaly alone or complicated by infection constitutes 90 per cent of the major problems in pediatric urology. Urogenital malformations tend to be multiple, and a thorough urologic examination is necessary to reveal the entire picture. They also are commonly accompanied by maldevelopment elsewhere, such as in the cardiovascular system, nasorespiratory system and other organs, so every child with a congenital anomaly in any one system must have a complete appraisal of the urinary tract.

Anomalies of the upper urinary tract (kidney, renal pelves, ureter) include a wide variety of disorders. For example, unilateral renal agenesia is encountered in about 1 in 550 cases. The single hypertrophied kidney is more likely to be the site of disease and especially of infection than are two normal kidneys. In the opposite kidney, which is usually hypertrophied, there may be reduplications of the pelvis or ureter, or it may occupy an ectopic position or include polycystic disease. Unilateral agenesia in the female may be accompanied by uterus unicornis or other uterine and vaginal abnormalities. Such abnormalities are usually detected following intravenous pyelography, but definite diagnosis can be made only after complete cystoscopic investigation.

Hypoplasia of one or both kidneys is noted in about 1 in 500 autopsies in children. It must be distinguished from secondary renal atrophy which has resulted from long-standing pyelonephritis, obstruction to the urine flow, or interference with the renal blood supply.

Congenital polycystic disease of the kidney is not rare. It occurs to some degree about once in every 250 births. In about one-third of such cases, far-advanced disease is present at birth and the children die of renal failure in the first year of life. The remainder of the cases may go undetected until the middle decades of life or even later, when a diagnosis of renal insufficiency on the basis of Bright's disease is frequently made. Polycystic disease is almost always bilateral, and some patients have accompanying cystic disease of the liver or spleen. This condition may also be associated with other anomalies of the urinary tract. It is usually detected either by palpating large nodular kidneys in the child's flank or as a result of urologic examination because of the appearance of symptoms of renal insufficiency, hypertension or, more likely, the presence of a urinary tract infection which is refractory to antibiotics. Pain, hematuria, pyuria or palpable mass may be present singularly or in combinations which lead to appropriate study and ultimate detection.

After proper recognition of congenital polycystic disease, treatment is directed toward the preservation of renal function as long as possible. This is accomplished by prompt treatment of any superimposed infection and correction of any coexisting obstructing anomaly. Proper chemotherapy or surgical intervention, therefore, may greatly prolong life. Some patients who live a life of moderation to decrease the demands on renal function and in whom infection and other complications are promptly treated may live into the latter decades.

Horseshoe kidney is one of the most common renal anomalies. The two kidneys are connected across the midline by a fused solid mass of renal parenchyma. Many horseshoe kidneys may be symptomless, but when this condition is present there is a remarkably high incidence of infection, stone or obstruction to the outflow of urine leading to hydronephrosis. The symptoms may be referable to these complications, or they may be characterized by chronic gastrointestinal disturbances, or epigastric or umbilical pain radiating to the lumbar area. Treatment in cases of horseshoe kidney is usually directed toward eliminating the complications such as calculus formation or obstruction. If infection is extensive on a single side, it may be necessary to divide the isthmus and remove half of an irreparably diseased kidney.

Ectopia or malposition of the kidney is a less frequent anomaly. The kidney may lie anywhere from the renal fossa to the pelvis. In complicated instances the two kidneys may be located on one side in which case they are usually fused, with the ureter from one pelvis

crossing to the opposite side of the bladder. Many combinations are possible, and such anomalies occur in about 1 in every 800 individuals, with a striking predominance among males. Most ectopic kidneys are deformed and abnormal in shape. Again they are clinically important, because they often are the site of infection, tumor or stone formation. In some instances they result in obscure abdominal pain in later life because of pressure on various other organs. The anomalous blood supply to some of these kidneys has been known to result in renal ischemia and hypertension. If urologic study is not carried out, a kidney located in the female pelvis may lead to the erroneous diagnosis of neoplasm of the female generative organs.

Anomalies of the renal vascular supply are extremely common, and anomalous variations from the highly variable normal pattern occur in 25 per cent of all adults. Anomalous vessels frequently encroach on the ureter and obstruct the urinary flow. The most common anomalies are accessory blood vessels crossing at the ureteropelvic junction, where they produce obstruction and hydronephrosis, often without symptoms. Symptoms when present rarely include pain, and they may be directed entirely to the gastrointestinal tract. Occasionally hematuria is the presenting symptom. Discovery of asymptomatic pyuria or a refractory urinary tract infection after full urologic survey often leads to the recognition of underlying hydronephrosis.

Hydronephrosis in many cases may be considered congenital in that many anomalies produce hydronephrosis as an end result. Severe hydronephrosis as a result of congenital obstruction has been noted in newborn infants. Pathognomonic symptoms are absent in hydronephrosis, and one-third of all patients have no symptoms referable to the urinary tract. Unfortunately, hydronephrosis too often is manifested late in the uremic stage. Symptoms sometimes mimic gastrointestinal disturbances, and hematuria may be the first. Chronic or refractory and recurrent urinary tract infections may call attention to the possibility of some underlying anatomic disorder in which hydronephrosis is discovered on urologic examination. Only rarely are acute obstructions simulating renal colic and associated with considerable pain and vomiting the presenting symptoms in a case of congenital hydronephrosis.

The most important feature of hydronephrosis is early recognition, following which the objective of management is restitution or preservation of renal function. The ultimate diagnosis is made by either excretory or retrograde urography and rarely by the palpation of the soft hydronephrotic mass in the region of the kidney. Corrective plastic surgery is required to relieve the obstruction, whether it be congenital vessels, stricture, abnormal valve formation, or any of a large number of other abnormalities. Relief of the obstruction leads to improvement of renal function if the parenchymal atrophy has not progressed to a terminal stage.

Many other anomalies of the renal pelvis and ureters too numerous to mention are found daily by urologists by means of either intravenous urography or retrograde pyelography. Reduplications of the renal pelves and ureters are extremely common. Congenital strictures of the ureter are a somewhat uncommon anomaly. These include congenital obstruction at the vesical neck, especially in the male child, atonic bladders and ureters, neuromuscular disease, posterior urethral valves, urethral diverticula, meatal strictures and various tumors. Either or both ureters may be duplicated, triplicated or involved in other anomalies such as ureterocele, postcaval ureter, congenital valve formations and ectopic terminations.

Obstructions leading to hydronephrotic atrophy and renal deterioration, which is often complicated and accentuated by infection, may occur from a vast number of causes and may be located anywhere from the renal pelvis to the urethral meatus in both the male and female.

Tumors of the Urogenital Tract

The introduction and widespread use of antibiotics for infections of the urinary tract and the prompt recognition and correction of various anomalies, obstructions, calculous dis-

ease, etc., have reduced the number of deaths from these disorders in children so that urinary tract cancer is now the second major cause of death between the ages of 1 and 14 years. The highly malignant nature of urogenital tumors in children places an even greater importance on early diagnosis. Benign tumors are relatively rare.

Almost all malignant tumors of the kidney in children are either embryonal carcinosarcomas (Wilms' tumors) or neuroblastomas. Wilms' tumor, containing heterologous tissue elements, grows very rapidly, but in spite of its high degree of malignancy it remains remarkably encapsulated until relatively late in the course of the disease. Three-fourths of the cases of Wilms' tumor occur before the age of five years and it rarely occurs after the age of seven years. Hematuria seldom is a presenting symptom. In most instances they produce no symptoms and are recognized only by the discovery of a mass as a result of careful abdominal palpation in the course of a general examination. The physician or pediatrician should palpate the renal areas in every child at every examination during the first years of life. When a child is brought in by his parents after they have discovered a large mass in the child's abdomen, the chances of cure are remote. Pain occurs only in older children, in about one-third of the cases, due to the weight of a large tumor or to pressure on adjacent organs. It is of interest that in about one-half the cases of Wilms' tumor the patients have an unexplained low-grade fever. In other cases hypertension is a curious feature.

If physical examination or symptoms suggest a renal tumor, intravenous urography supplemented by retrograde pyelography is imperative to make a definite diagnosis. The neoplastic elements in these tumors tend to grow into the venous spaces, and a fragment may easily be dislodged into the blood stream from unnecessary or rough preoperative palpation. Most Wilms' tumors are radiosensitive and are greatly reduced in size by preoperative radiation. The cure rate is in direct proportion to the stage at which the diagnosis is made. Cure is possible in 40 to 50 per cent with early detection followed by prompt surgery and thorough roentgen therapy.

Another common tumor in the renal area, one which usually is located just above the kidney instead of within the kidney, is neuroblastoma. This tumor originates from nerve elements and may tend to displace the kidney downward without producing the pyelographic deformity found in Wilms' tumors. Neuroblastomas tend to metastasize to bone, and these metastases sometimes are detected before the flank tumor is diagnosed. Treatment is the same as for Wilms' tumor.

Other malignant tumors in children are less important because of their relative infrequency. Epithelial tumors of the bladder are extremely rare. Most malignancies of this organ are sarcomas which grow so rapidly to fill the entire bladder that only a few cures have been recorded. Their initial symptoms are urinary frequency, dysuria, incontinence and even enuresis. The diagnosis generally can be made by bimanual rectal examination. Prostatic tumors in children are also rare and are always sarcomas, highly malignant and generally incurable. Epithelial carcinoma of the prostate as seen in the adult male has not been observed in children. Penile tumors are extremely rare in children. When circumcision is performed at birth, cancer of the penis in the adult almost never occurs.

Testicular Tumors

Testicular tumors are quite rare in children and are generally of the teratoid type in contradistinction to the frequently encountered seminoma in adults. Unfortunately, the early stages are often overlooked because of the smallness of the nodule in the testes and because of its asymptomatic nature. Diagnosis may be obscured by an accompanying hydrocele which must be aspirated to facilitate careful palpation of the testis. In too many cases the tumor is discovered only after the appearance of a large metastatic upper abdominal mass.

Neuromuscular Disease

Although seen relatively infrequently, neuromuscular diseases leading to atony of the urinary tract are important because of their

insidious onset and the severe renal damage which usually ensues. The latter results from a combination of obstruction leading to hydronephrosis and superimposed secondary infection, both of which progressively destroy the kidneys. Atony of the ureter or megalo-ureter is generally a congenital defect due either to disease of the spinal cord (spina bifida) or to some defect in the parasympathetic nervous system resulting in defective peristalsis. It is thought to be similar in many respects to Hirschsprung's disease in the bowel, in about 50 per cent of which cases there is concomitant atony of the upper urinary tract.

If the dysfunction involves the bladder, urinary incontinence or enuresis may be the presenting symptom. In general, however, detection results during the course of a chronic urinary tract infection. Vesicoureteral reflux is a common finding; because of an inadequate vesicoureteral valve, the intravesical voiding pressure is transmitted to the kidney, leading to back pressure and hydronephrosis complicated in most cases by episodes of relentless pyelonephritis. Treatment is directed toward relief of any urinary obstruction at the vesical neck or urethra, reimplantation of ureters into the bladder to control reflux, and chemotherapy for eradication or at least control of the superimposed bacterial infection. Various parasympathomimetic drugs may also help in some cases.

Calculous Disease

Urinary calculous disease occurs relatively rarely in infants and children in this country. Most stone formation in childhood probably has a nutritional basis, in the absence of congenital anomaly or urinary stasis, and results from some deranged metabolism. Thus, most stones are composed of uric acid and urates. Pure uric acid stones are not radiopaque, and as a result some cases of calculous diseases have been diagnosed and treated as chronic pyelitis. Most children in whom renal calculi develop have urinary tract infection by the time correct diagnosis is made. In other words, 9 out of 10 cases of urinary calculous disease in children are eventually and correctly diagnosed because of examination for persistent or recurrent pyuria. The ultimate diagnosis and treatment in children are identical to those in adults.

Enuresis

Any discussion of pediatric urology should include the ever-present problem of enuresis. This frequent and perplexing disorder generally falls into two categories: (1) *true* enuresis, which is functional or psychogenic in origin, and (2) *secondary* enuresis, which is a result of some definite underlying disorder or disease. True enuresis is considered a personality or conduct disorder which usually originates in the subconscious mind, commonly as a resentment toward the parents or home environment in which the child responds to the subconscious urge to return to the protected environment of infancy.

A careful history and a urinalysis are necessary in every case of enuresis, and the physician should assume that an underlying abnormality is present until he proves otherwise. If no underlying abnormality can be found, medical or psychiatric treatment is justified. Half the patients who do not respond to such treatment are said to have associated organic lesions of the urinary tract. The most important feature is to determine whether or not there is any underlying anatomic disease in the urinary tract or in the central nervous system.

There is no specific medical treatment for true or functional enuresis. Treatments which have been suggested include revision of the child's home life and his relationship to his parents, proper diet, and good sleep habits. Most important, the physician must acquaint the parents with the probable underlying emotional causes and emphasize the importance of minimizing their own emotional reaction to the child's bid for their attention. Supplementary methods may include limitation of fluids at night and administration of parasympathicolytic (PRO-BANTHINE®) drugs to reduce the nocturnal bladder tone. In males, a brief course of therapy with androgens develops the musculature of the prostatic urethra and often relieves the bed-wetting. Development of conditioned reflexes by means

of clocks and bells which awaken the child at night and correct toilet training is occasionally successful. All efforts should be directed toward correcting the underlying personality disorder in the child, in siblings and even in the parents, who are often the culprits. Proper management usually includes a thorough search for either organic, urologic or neuromuscular disease, of which enuresis may be the only symptom.

Summary

A few common urogenital disorders in children have been briefly reviewed. These disorders, especially infections, anomalies and tumors, must be kept in mind when urinary abnormalities or disturbances are encountered in children. An early and correct diagnosis is of primary importance, because the absence of symptoms is a striking feature. A high index of suspicion directed toward the urinary tract followed by careful urologic examination may lead to early diagnosis and intelligent management of underlying urogenital disorders. This, in turn, may allow many children who otherwise would die in the first decade of life, or many adults who are suffering the dire consequences of a disorder present since childhood, to live a normal life span.

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Postgraduate Clinical NOTES

28. THE ABUSE OF REST

Consider further the widespread belief that hard work, with its mental and physical activity, plays an important part in the causation of disease. This belief has little rational basis; it does not rest on a critical analysis of the physiology of activity; and it is not attached to any demonstration of damage by repeated muscular contraction, by the elevated metabolism of effort, or by concentrated thought. Indeed there is abundant evidence that none of the known effects of work can harm healthy tissues. On the contrary all these effects are, in a different context, regarded as beneficial in the sense that they develop and extend the range of adaptation of physiological mechanisms.

The evil reputation of work as a cause of disease springs from two rather disreputable and quite illogical traits in human character. The first is the widespread reluctance of medical men to admit frankly that they are ignorant of the cause of disease—that they do not know why a particular person has fallen victim to an infection or why another person's blood pressure has risen or a clot formed in his coronary artery. The second is the very understandable but really quite indecent avidity with which a patient accepts the explanation that his illness is due to overwork and insufficient rest. It is a belief which nourishes his *amour-propre;* it enrols him in the noble army of martyrs; he has fallen fighting the good fight. Believing this, he can relax with a clear conscience and enjoy to the full the provisions of a Welfare State, the bondage of a possessive wife, and the plaudits of an admiring family.

W. Melville Arnott, *The Lancet,* June 19, 1954, p. 1251

Immunization Against Communicable Diseases in Childhood

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In the last four decades the value of immunization against certain communicable diseases has been impressively demonstrated by a decrease in the morbidity and mortality rates. Immunization first was used successfully against smallpox and subsequently against rabies. In 1798 Jenner[1] discovered that material obtained from the lesions of cowpox (cowpox virus) could be substituted for material obtained from the lesions of smallpox in immunizing persons against this disease. At present a vaccine prepared from the virus of cowpox (vaccine virus) is being used almost universally. Since little was known about the viruses until the last decade, it is surprising that smallpox was the first communicable disease to be controlled by immunization.

In the nineteenth century it theoretically seemed possible that bacterial antigens might stimulate the formation of antibodies, but it remained for Ramon[2,3] and some of his contemporaries, notably Park,[4] to prove that this theory was correct.

Toxin-antitoxin and toxoid** have been successfully employed to immunize children against diphtheria, and tetanus toxoid has proved effective in protecting children against this disease. Diphtheria toxoid and tetanus toxoid can be administered in combination, and they act synergistically when administered in this manner. Although fluid toxoids are available, alum-precipitated toxoids generally are used.

Vaccines have been effective in producing immunity to a number of diseases, particularly pertussis and diseases of the typhoid-paratyphoid group. In immunization against pertussis the regular pertussis vaccine (pertussis vaccine U.S.P.) or alum-adsorbed pertussis vaccine is generally used.

Smallpox

Smallpox vaccination has been performed

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**In 1916, Ramon used the term anatoxin to designate a toxoid, and this term still is being used in Europe.

on infants and children as well as on adults. There is no arbitrary limit to the immunity produced by the vaccination. In many states the laws require that all children must be vaccinated against smallpox before they enter school. Unfortunately in some communities these laws have caused parents to conclude that vaccination should not be performed before their children become old enough to start school. Health officers, physicians and social workers frequently have not stressed the advantages of vaccination at an earlier date. Fortunately this attitude has been reversed as a result of the increased interest in the prevention of disease.

The most favorable time for primary vaccination against smallpox is in infancy or even in the neonatal period. Experience seems to indicate that the duration of the immunity produced by vaccination at this time lasts longer than that produced by vaccination at school age. When vaccination is performed in infancy or in the neonatal period, systemic reactions occur less frequently than they do when it is performed later, and when such reactions do occur they usually are less severe. Postvaccinal encephalitis does not occur in cases in which children are vaccinated before they are one year old. The only contraindications to vaccination at this age are serious debility and the presence of a skin lesion, such as eczema, which has caused a break in the skin. If vaccination is performed when a lesion of this type is present, vaccinia and secondary infection are likely to occur and the child may die.

In immunization against smallpox, one of the following methods generally is used: (1) multiple pressure method, (2) the single scratch method, or (3) intradermal inoculation. Regardless of which method is used, the site selected for the vaccination should be washed thoroughly with soap and water and dried with sterile cotton. Alcohol then should be applied and permitted to evaporate. Dressings are unnecessary after vaccination. Since vaccination shields promote moisture, heat and congestion, and thus increase the likelihood of infection, including possibly tetanus, their use is contraindicated.

The multiple pressure method is used more frequently than either of the other two methods. A drop of vaccine is applied to the skin. Pressure is applied to the underlying skin with a needle which is held parallel to the skin and moved rapidly up and down. The trauma is caused by the side of the point of the needle. Since bleeding is less likely to occur when this method is used, it is believed that "takes" will be obtained more frequently than they will with either of the other two methods. Multiple vaccinations frequently occur in cases in which this method is used.

When the single scratch method is used, the vaccine is placed on the skin and a scratch about 1/8 in. long is made on the underlying skin. By using the flat side of the needle the vaccine is rubbed into the scratch until the edges become puffed and ischemic. The excess vaccine is wiped off with sterile cotton. Multiple vaccinations seldom occur when this method is used. The puffiness and ischemia of the edges of the scratch indicate that the virus used in preparing the vaccine was a potent one and that the vaccination will take in primary vaccinations but not in secondary vaccinations in immunes. The resulting scar will not be any larger than a 10 cent piece.

Intradermal inoculation is rarely used, and it does not have any advantages over the other two methods. Since it ordinarily does not produce any scar, school authorities and quarantine officers in foreign ports frequently reject certification of vaccination performed by this method.

If the parent of a child who has been vaccinated in infancy or in the neonatal period should ask when the child should be vaccinated again, he should be told that the vaccination should be repeated at school age or at any other time when the child has been exposed to smallpox. If a patient asks whether or not he should be vaccinated he should be advised in the affirmative. If the vaccination takes, it was needed. If it does not take, or if it produces an immune reaction, no harm will have been done and the question will have been answered.

If a second vaccination is followed only by a local reaction it indicates that the person is

immune to smallpox. This reaction may consist of a small macule which appears within 24 hours. In some cases a papule may appear within 72 hours, a vesicle may occur within five days, or a small pustule may develop within seven days. I have discharged hundreds of persons who had been quarantined because they had been exposed to smallpox and whose vaccination was followed by an immune reaction. Smallpox did not develop in any of them.

Diphtheria

In practically all diphtheria immunization programs, diphtheria toxoid and tetanus toxoid are administered in combination. After primary injection of a single dose of diphtheria toxoid the antitoxin titer of the serum increases slowly and steadily for some time. Bigler and Werner[5] reported that the maximal response occurred three months after the injection, but my experience indicates that it does not occur before six months. Edsall, Banton and Wheeler[6] observed little change between the titer determined three weeks after inoculation and that determined five months later.

A second injection of toxoid, regardless of when it is given, is followed by a temporary increase in the titer. This will be followed by a decrease but the titer will not drop to its former maximal level. It then will rise to a new maximal level within six months. When three injections of toxoid are given at intervals of one month, the antitoxin titer does not become as high as it does when two injections are given six months apart.

Several authors have recommended that the amount of antigen in toxoid preparations be increased. According to Christie and Peterson,[7] such an increase would have the following advantages: (1) it would result in a sounder basic immunity, and (2) it would decrease the need for repeated administration of booster doses of the toxoid. I do not believe that increasing the antigen content is sufficient in itself since the reduction in the quantity of alum deprives the patient of much of the "depot immunization" that provides longer and higher limits of immunity and increases longevity of immunity.

There is a growing tendency to use diphtheria immunization before the sixth month despite the fact that passive immunity transmitted by the mother may still be present. I agree with Christie and Peterson[7] who said, "When the degree of passive immunity is minimal, the response modification is also minimal, but when the degree of passive immunity is high the primary response is very poor." In infants with a high degree of passive immunity there is an inhibition of the capacity to respond to secondary immunization as well as a failure in the primary response.

The theory that the capacity to respond to antigenic stimuli is a distinct phase of physiologic maturation is not supported. According to Christie and Peterson,[7] "The capacity of even very young infants to respond to diphtheria toxoid is such that they may be successfully immunized and their immunity will be adequate if the primary vaccination is followed by a recall injection after 10 to 15 months."

Since immunity to diphtheria develops slowly after primary injection, it is evident that infants who are immunized when they are two or three months old will receive very little protection during the next few months. The response to injection before this period is not worth considering. Pearlman[8] could not find that early immunization against diphtheria had any effect on the mortality rates of this disease in Canada.

I prefer to inject the toxoid into the deep subcutaneous tissues. When this method of administration is used the antitoxin titer is higher at the end of six months than it is when the toxoid is injected intramuscularly. Since an abscess occasionally occurs after subcutaneous injection, intramuscular injection has been used more frequently. I have never observed a case in which such an abscess occurred. Abscesses can occur only when the product used is contaminated or when the bottle has not been shaken and the last doses therefrom are concentrated alum injections. Incidentally, there is no immunizing agent left in the alum and the first doses amount to nothing more than a fluid toxoid injection. Fluid toxoids do not produce the immunologic

response that alum-precipitated toxoids do.

The best procedure known to date is to inject both diphtheria toxoid and tetanus toxoid when the child is six months old and to repeat the injection six months later. A third injection can be given when the child is six years old.

Since immunity is only relative, one is justified in attempting to determine as nearly as possible the degree of immunity that has been produced in an individual case. The Schick test for diphtheria is the only approach to this problem from the clinical standpoint. Inaccuracies in technic have caused some physicians to reject this test, but it is reliable if it is performed correctly, if the result is read at the *end* of 72 hours, and if a control test is performed. The Schick test should be performed six months after the second injection.

It is an established fact that exposure to the toxin of diphtheria through carriers of *Corynebacterium diphtheriae* or persons who have the disease will cause a rapid increase in the antitoxin titer of the serum of persons who are immune or partially immune to the disease and that this increase will parallel that which occurs after follow-up injections of diphtheria toxoid or toxin-antitoxin. A similar increase also occurs after a Schick test is performed. Since the incidence of diphtheria has declined, the carrier problem has decreased, and a stimulation of antibodies rarely is attributable to exposure through carriers.

In panel discussions I have heard speakers assert that 40 per cent of adults now are susceptible to diphtheria, but no authority for this assertion was quoted. If this assertion were true, diphtheria should be classified as an adult disease. On the contrary, it is comparatively rare among adults. It is interesting to speculate whether or not persons who have been stimulated to produce antibodies would be automatically immunized by exposure to the disease.

The belief that immunity to diphtheria is of short duration has prompted some authors[9] to recommend injection of diphtheria toxoid every three years in order to maintain the immunity. I cannot agree with this recommendation. In cases in which a Schick test reveals that immunization has produced an effective immunity, and even in cases in which the result of a second test is positive, any absorption of diphtheria toxin will produce a rapid antibody response. This response may occur many years after the original immunization.

Approximately 20,000 children who lived in urban communities were immunized when they were infants and again when they were six years old. A Schick test was performed when they reached the age of 18 years, and the result of the test was positive in less than 100 instances. Since diphtheria is a rare disease, triannual recall injections would be distinctly unnecessary. In the event of exposure a recall injection or exposure itself could be relied on to give prompt immunity.

If there has been no effort made to immunize actively against diphtheria and exposure takes place, then diphtheria antitoxin should be given in doses not smaller than 5000 to 10,000 units.

Tetanus

There is no simple test which will determine whether or not a person is immune to tetanus. In cases in which an accident indicates the need for tetanus prophylaxis, a recall dose of tetanus toxoid can be given if it is definitely known that this preparation has been administered previously. Otherwise, tetanus antitoxin should be used although there is some doubt as to its efficacy.

In adults, alum-precipitated tetanus toxoid is likely to cause a severe reaction. In such cases the less efficient fluid toxoid can be used. Since the reaction caused by the alum-precipitated toxoid is much less severe than tetanus, this preparation should be used whenever possible.

In recent years alum-precipitated tetanus toxoid, alum-precipitated diphtheria toxoid and alum-adsorbed pertussis vaccine have been administered in combination to immunize children.

Pertussis

After administration of any type of pertussis vaccine, immunity, if it develops at all, does so rapidly and lasts for approximately

two years. As previously stated, alum-adsorbed pertussis vaccine recently has been administered in combination with alum-precipitated tetanus and diphtheria toxoids. When these immunologic agents are administered in this manner they do not act synergistically as do the tetanus and diphtheria toxoids when they are administered together. There is a decrease in the effectiveness of the diphtheria and tetanus toxoids or in that of the pertussis vaccine.

Pertussis vaccine produces a severe reaction, particularly when it is administered in combination with tetanus and diphtheria toxoids. It causes convulsions in some cases and there are authentic reports of cases in which it has caused death. It has been asserted that convulsions which have been attributed to the administration of the vaccine undoubtedly would have occurred if the vaccine had not been administered and if pertussis had developed. Naturally, there is no proof for this assertion.

In order to prevent reactions as far as possible, three injections of pertussis vaccine should be given at intervals of one month. There is no real objection to administering diphtheria and tetanus toxoids and pertussis vaccine independently. When this procedure is used a dose of each of these immunologic preparations is administered on the same day at different sites, and two subsequent doses of the pertussis vaccine are administered at intervals of one month. Subsequent doses of the diphtheria and tetanus toxoids are not given until six months after the initial injection.

As has been stated previously, all immunity is relative. Peterson and Christie[10] have said that three injections of alum-adsorbed pertussis vaccine at intervals of one month will produce a protective level of immunity in 77 per cent of infants and children. If the antigenic content of the vaccine could be increased and if the incidence of reactions could be decreased, the use of this vaccine might produce really good results. It is hoped that the use of this vaccine will modify the course of pertussis if it should fail to immunize in a given case.

Many physicians have recommended that infants should be immunized against pertussis before they are six months old, but there are several obstacles to this procedure. The foremost of these is the passive immunity which is transmitted through the placenta. This is operative in greater or lesser degree until the infant is six months old. If the infant is breast-fed the antibody titer of the serum will be augmented by the passage of antibodies through the milk. Under such circumstances an antibody response either will not occur or will be very feeble.

Peterson and Christie[10] have said that passive immunity resulting from the passage of antibodies through the placenta not only interferes with the development and maintenance of a high antibody titer but also inhibits the development of a capacity to respond to secondary immunization. Cohen and Scadron[11] have tried to immunize newborn babies by attempting to immunize expectant mothers with pertussis vaccine in the last trimester of pregnancy. They said that further study is necessary to determine the persistence of the antibodies that are transmitted to the infant. There is no reason to believe that there is any difference in behavior in passive immunities.

Pearlman[8] said that two months will be required for the development of immunity if three injections of pertussis vaccine are given at intervals of one month and that if injections are started in the first month they will produce an effective immunity in only about 60 per cent of the infants. About half of these infants will have lost their protective immunity within a few months. He said that, although immunization before the age of six or seven months might have had a favorable influence on the mortality rate of pertussis in Canada, the improvement has not been sufficient to encourage any enthusiasm for immunization at this age.

Perhaps a workable compromise would be to give pertussis vaccine at the age of one, two and three months if the infant is likely to be exposed to the disease by older children living in the same house. Otherwise the vaccine should not be given until the sixth month. Parents always should be told that the vaccine is likely to cause a reaction. They should be given an opportunity to decide whether or not it should be given.

Typhoid and Paratyphoid Fever

The universal immunization of children against typhoid and paratyphoid fever is worthy of consideration. Almost all children may be exposed to these diseases through food handlers and contaminated water supplies, and especially when they begin to swim, or to go to summer camps and to church picnics and suppers. In some communities the incidence of typhoid fever is much lower than it is in others. This is attributable to immunization and good sanitation.

Three injections of typhoid and paratyphoid vaccine may be given at intervals of one week when exposure is possible. The resulting immunity will last for two years and it may be expected that the child will be partially protected for another year. Typhoid-paratyphoid vaccine as referred to here contains in each cubic centimeter:

Typhoid bacilli *(Salmonella typhosa)* 1000 million.

Paratyphoid bacilli A *(S. paratyphi)* 250 million.

Paratyphoid bacilli B *(S. schottmülleri)* 250 million.

In childhood each dose is determined by the fraction formed by the weight of the child divided by 150. A 50 pound child would therefore receive ⅓ of 1 cc. These injections are administered *subcutaneously*. Immunization may be repeated every two or three years by injecting a single dose of 0.1 cc. of the above triple vaccine *intradermally* or by giving three *subcutaneous* injections as given primarily. I have found the former plan to be very efficient.

Immunization Against Other Diseases

Effective preparations are available for immunization against cholera, yellow fever and Rocky Mountain spotted fever, and one for immunizing children against poliomyelitis may be in the offing. These immunologic agents for the most part have a regional rather than a universal application. They should be administered in regions in which the respective diseases are prevalent. Antirabic vaccine should be given to any child who is believed to have been exposed to rabies.

Universal Immunization Program

The following immunization program is recommended for universal use:

1. Smallpox vaccination should be performed between the first and tenth months.
2. Diphtheria and tetanus toxoids should be given at six months.
3. Beginning at the seventh month, three injections of pertussis vaccine should be given at intervals of one month.
4. Injection of diphtheria and tetanus toxoids should be repeated at the twelfth month.
5. A Schick test should be performed at the eighteenth month. If the result of the test is positive, another injection of diphtheria and tetanus toxoids should be given.
6. At six years, another injection of diphtheria and tetanus toxoids should be given, smallpox vaccination should be repeated, and typhoid and paratyphoid vaccine should be administered.
7. Administration of typhoid and paratyphoid vaccine should be repeated every two or three years when the child is between 6 and 18 years of age.
8. A Schick test should be performed at 18 years. If the result of the test is positive, fluid diphtheria toxoid should be given.
9. Vaccination against smallpox should be performed whenever a child has been exposed to the disease or is going to travel where the disease is known to exist.
10. Tetanus toxoid should be administered whenever a child has an open or penetrating wound that is likely to become infected with *Clostridium tetani.*

Immunization Records

Every physician should keep a record of the immunizing procedures used in each case. This record can be kept on a folded card. The name of the child and the date of birth should be inscribed on the outside of the card. Vertical columns on the inside of the card should be provided for the following headings: smallpox, diphtheria, pertussis, typhoid fever and the Schick test. Whenever a Schick test is performed, the result of the test should be recorded. The type and date of each immunologic procedure should be recorded in the

proper column and the physician should sign the card on each occasion. The obligation to provide such a record and keep it up-to-date is just as great as providing a copy of the birth certificate. It is particularly important to provide such a record in cases in which the patients are transients.

Summary

All children should be immunized against smallpox, diphtheria, tetanus, and perhaps against pertussis, in accordance with a definite program. An increase in the antigenic content of the immunologic preparations would increase the effectiveness of the immunization. This is particularly true in regard to pertussis vaccine.

Although effective preparations are available for immunization against several other communicable diseases, they have a regional rather than a universal application. They should be administered in regions in which the respective diseases are prevalent.

Physicians should keep a record of all immunization procedures employed, and this record should be kept up-to-date.

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Postgraduate Clinical NOTES

29. STANDARDS FOR LOW SALT DIETS

An amendment of the dietary foods labeling regulations under the Federal Food, Drug and Cosmetic Act, the Food and Drug Administration, U. S. Department of Health, Education and Welfare, establishes a new regulation for labeling "salt free" or "low sodium" food products for dietary use. Sodium content must be declared in milligrams of sodium per 100 gm. of the food, and in an average serving of the food. The "average serving" is required to be expressed in such common terms as the number of slices, cookies, wafers, etc., or in terms of cupsful, tablespoonsful, teaspoonsful, etc.

Many products were found on the market labeled "salt free" or "no added salt" but which nevertheless contained substantial amounts of sodium, naturally present as in some vegetables, or added in the form of baking powders or other ingredients. The new regulation should insure uniformity in the label information regarding the salt or sodium content of the foods and make it possible for patients better to compute their intake of sodium.

The regulations are in line with recommendations made by the American Heart Association and the Council on Foods and Nutrition of the American Medical Association.

U. S. Department of Health, Education, and Welfare
Food and Drug Administration

Diagnosis and Treatment of Hypothyroidism

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PAUL STARR

EVERY diagnosis obviously results from a presumption that the condition to be demonstrated might exist. If the suspicion fails to occur to the physician's mind, the necessary steps are not taken. Unfortunately, hypothyroidism has been so confused with myxedema that the possibility of hypothyroidism is not considered with nearly the frequency that the incidence of the disease warrants. Myxedema is a state of the tissues which frequently causes symptoms that produce a striking clinical picture. It is, however, a rather rare syndrome. For every patient with clinical myxedema there must be at least a hundred patients with hypothyroidism *sine* myxedema. This requires a broadening of clinical concepts of hypothyroidism so that the diagnosis can be made more frequently. The presence of hypothyroidism should be suspected in:

1. Children who fail to grow.
2. Delayed puberty.
3. Menstrual disorders, such as menorrhagia and amenorrhea.
4. Anovulation, infertility and habitual abortion.
5. Mastalgia and cystadenosis of the breast.
6. Some cases of obesity.
7. Gastrointestinal syndromes such as peptic ulcer, hypochlorhydria, functional hypoglycemia and constipation.
8. Chronic fatigue, anorexia, leanness or neurasthenia.
9. Some cases of anemia.
10. Disturbances of the ectoderm such as dry skin and alopecia.
11. Allergic syndromes.

In such cases the patients may have severe hypothyroidism without the mental sluggish-

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ness, anemia, sensitivity to cold, large tongue, croaking voice, and easy-going negativism of myxedema.

Should this broader concept of hypothyroidism be accepted by the physician, he will often act to establish the presence of the disorder by determination of the basal metabolic rate. It can be easily demonstrated that this has, as often as not, deceived him into believing that the thyroid function of the patient was normal. For in all these conditions emotional reactions are labile, and a truly low basal metabolic rate may be elevated to normal by nervousness during the test. The results of a typical series of determinations of the basal metabolic rate in a case of gross athyreotic hypothyroidism are shown in figure 1. It may be seen that preliminary determinations were done as training tests before a true basal level of metabolism was demonstrated. If a patient with subclinical hypothyroidism had a true basal metabolic rate of −30 per cent, transient nervousness could easily raise the rate to −10 per cent and the presence of basal hypometabolism would be concealed.

A few examples of this discrepancy between the results of first and second tests on ambulatory patients are shown in figure 2. It is evident that the normal results of the initial tests on two of these four patients (Mr. R. C. and Mrs. W. O.) concealed the presence of serious hypometabolism. It is understood, of course, that the cause of the hypometabolism in these patients can only be discovered by biochemi-

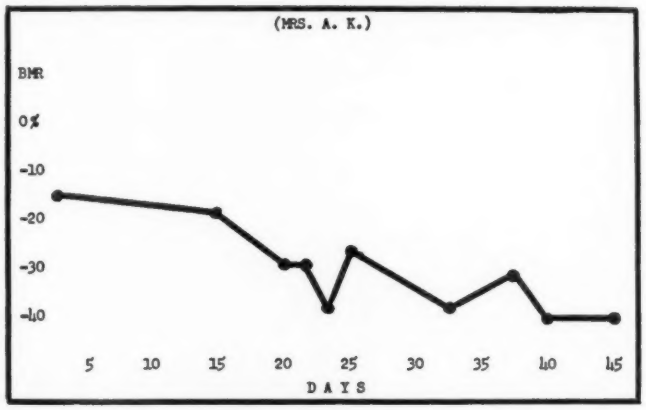

FIGURE 1. Results of a series of basal metabolic tests in a case of athyreotic hypothyroidism. Eight successive tests were required to train the patient to respond properly to the tests. After the forty-fifth day, the basal metabolic rate was −40 per cent on several occasions.

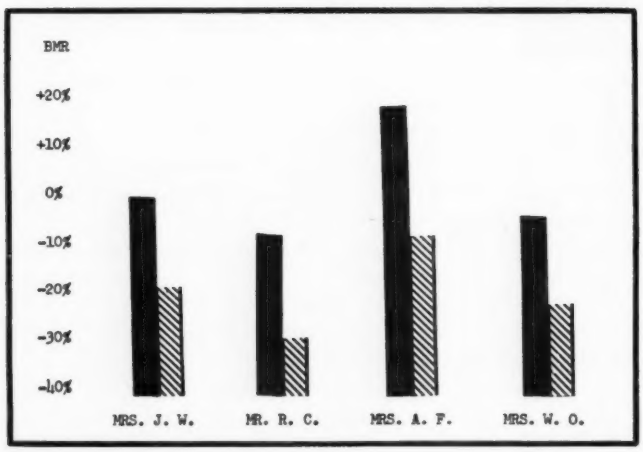

FIGURE 2. Results of first (black) and second (crosshatched) tests of the basal metabolic rate of ambulatory patients. Note the marked discrepancy. Significant hypometabolism is revealed in three of the four patients. The initial test on the three patients revealed a normal basal metabolism.

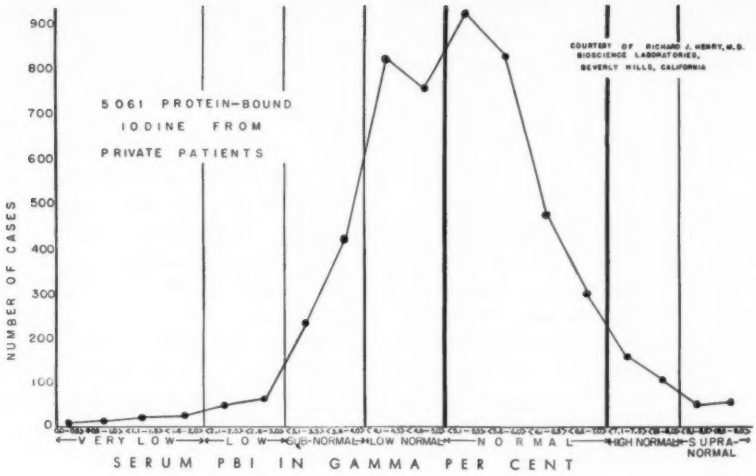

FIGURE 3. Results of determination of serum protein-bound iodine in specimens submitted within less than one year by private physicians.

cal measurements. Hypometabolism is by no means hypothyroidism. It is probably this dependence on the basal metabolic test and a failure to realize the nervousness of hypothyroid patients that has so long prevented the diagnosis of hypothyroidism in a large number of cases.

It is thus seen that in the use of screening tests to detect a common disorder with protean characteristics one must select a test with pathognomonic quality. Such a test is the determination of the protein-bound iodine in the serum, which costs the patient in many cities somewhat less than the unreliable, usually fallacious basal metabolic test. If it should be admitted that at least three successive basal metabolic tests are necessary before an approximation of the patient's hypometabolism can be obtained, the cost of the metabolism test becomes more than three times that of the single serum protein-bound iodine test, which gives pathognomonic biochemical information. The chemical test estimates the circulating thyroid, namely, thyroxin, in protein combination. In skillful hands this may be done with an error of less than 10 per cent.

The results of 5,061 determinations in a private laboratory and 2,178 determinations in a municipal hospital laboratory are shown in figures 3 and 4. The method used was the Ware modification of the Barker method.[1] This procedure may be carried out in a general chemical laboratory by a regular laboratory technician without unusual avoidance of iodine in the atmosphere. It is true that, as in all exact chemical determinations, constant inner control of the quality of reagents and the reliability of the procedures must be checked frequently.[2] The normal range for this determination of thyroid function is from 5 to 7 μg. per 100 cc. of serum. The normal values have been stated to range from 3.5 to 8.5 μg. per 100 cc. This is to be attributed to the fact that the persons in the selected groups actually were not physiologically normal.

Artefacts are created by the ingestion of medicine containing iodine in large amounts, and by roentgenographic dyes. This effect occurs whether the medicine contains inorganic iodide or iodine in organic combination. These substances also falsify the determination of the uptake of radioactive iodine by the thyroid gland. The usual amount of iodine in the normal diet, including sea food or iodized salt, is not sufficient to falsify the protein-bound iodine determination of the circulating

thyroid hormone. If the distillation method of determination is used, as in the Chaney method, the administration of mercury blocks the procedure, so that a falsely small value is obtained. With these considerations in mind, the single protein-bound iodine determination becomes the most reliable method of estimating the thyroid function of the patient.

The availability of radioactive iodine and the ease of measuring radioactivity have led to a large variety of diagnostic methods of thyroid function. It must always be remembered, however, that these procedures usually deal only with the relation of the thyroid to iodide metabolism, and that they rarely have to do with the production of the thyroid hormone. For example, the thyroid gland saturated with iodide, as after treatment with potassium iodide, will have negligible uptake of I^{131}, but will be producing excessive amounts of hormone. Under these circumstances the isotope uptake tests would be giving a false low value. Vice versa, in cases of cretinism associated with large goiters the uptake of radioactive iodine may be in the high supernormal range,[3] which might be interpreted as indicating an increased amount of hormone production when, in fact, the goitrous gland is unable to make any thyroid hormone.[4] The effect of iodide or iodine medication, which was discussed in connection with the protein-bound iodine measurement, must be considered in the same way when the isotope test is used. In general, the I^{131} tests are more reliable in demonstrating hyperthyroidism than they are in demonstrating hypothyroidism, because many normal people with good iodide metabolism may take up a relatively small amount of isotope, and in some cases of severe hypothyroidism, with avid epithelium, the uptake of radioactive iodine may be nearly normal.

In the diagnosis of hypothyroidism especially, the I^{131} tests should be used conservatively. The measurement of the rate of excretion and amount of isotope appearing in the urine after administration of a tracer dose seems to be a reliable test for hypothyroidism, but the effects of renal function must always be evaluated.[5] Clark, Moe and Adams[6] and, subsequently, Morton[7] have used the incorporation of the inorganic I^{131} into the organic iodide-protein-bound iodine component of the serum as a measurement of thyroid function, and this is a good indication of hormone production. The procedure, however, again rests on the determination of the organic iodine in the serum and thus it is more complicated, although useful and informative. This test also is more reliable and more valuable in the diag-

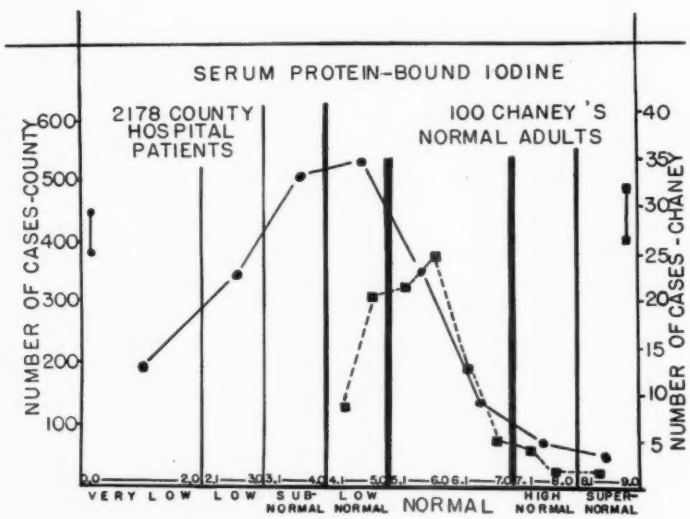

FIGURE 4. Values for serum protein-bound iodine found by laboratory technicians in samples submitted from the wards and clinics of the Los Angeles County Hospital in 1952.

nosis of hyperthyroidism, and less reliable in the demonstration of hypothyroidism.

Hypothyroidism may be classified etiologically as follows: (1) athyreotic, (2) hypopituitary, (3) hypothalamic and (4) somatic.

This classification is intended to point out that the reduced amount of thyroid hormone being supplied to the tissues, which creates the clinical state, may be variously caused. The first, but not the most common cause of hypothyroidism is a defect in the gland itself. It may be the site of an intrinsic disorder that reduces the production of thyroid hormone. This is probably the case in endemic goitrous cretinism and in colloid goiter. The thyroid may not be receiving adequate amounts of iodide for the formation of thyroid hormone. More commonly, the thyroid is subject to idiopathic atrophy, which creates a clinical state that might be called the thyropause. Finally, the thyroid may have been removed by operation or radiation therapy. For whatever reason, the failure of the tissue to receive thyroid hormone is, in this classification, dependent on the thyroid gland.

Hypopituitary hypothyroidism is more common than athyreotic hypothyroidism. In this type, the thyroid gland is able to make the hormone, but is not kept at an adequate rate of production by sufficient anterior pituitary thyrotropic hormone. This may be associated with total destruction of the pituitary body, as in Simmonds' disease, or by partial destruction of the pituitary body in Sheehan's syndrome, which is far more common, or in functional hypopituitarism.

Monohormonal hypopituitarism, confined to the thyrotropic hormone, has been reported, and idiopathic polyhormonal hypopituitarism associated with disorders of the gonads and adrenal glands, as well as the thyroid, is a relatively common condition.

Hypothalamic hypopituitarism has been much more rarely demonstrated but has not received adequate clinical study. Earlier references to the occurrence of endocrine disorders, including myxedema after encephalitis, have been made in the literature.[8]

The somatic type of hypothyroidism is that associated with nephrosis or other disorders, usually involving the blood proteins that are required for the transportation of thyroxin. It has been shown in nephrosis that the protein-bound iodine is as low as the albumin of the serum.[9] In other states of hypoalbuminemia, the value for the protein-bound iodine may be normal.

Another classification of hypothyroidism which is based on the amount of circulating thyroid hormone is shown in table 1. Adherence to this classification is very useful in general medical practice. It requires careful biochemical work so that the margin of error of the individual determination of the protein-bound iodine is well controlled.

The distinction of the athyreotic from the hypopituitary form of hypothyroidism is now easily made by the use of thyrotropic hormone.* The uptake of radioactive iodine and the value for the protein-bound iodine are determined before administering three successive daily doses of 10 mg. of anterior pituitary thyrotropic hormone, following which, on the fourth day, the uptake of radioactive iodine and the value for the protein-bound iodine are again determined. In cases in which hypothyroidism is due to inactivity or unproduc-

*THYTROPAR®, which is used for this test, is made by the Armour Laboratories, Inc., of Chicago, Illinois.

TABLE 1

CLASSIFICATION OF HYPOTHYROIDISM AND HYPERTHYROIDISM

TYPES	CIRCULATING THYROID HORMONE
Myxedema	Very low—0 to 2 μg. per 100 cc. of serum
Severe hypothyroidism	Low—2 to 3 μg. per 100 cc. of serum
Moderate, often hypopituitary hypothyroidism	Subnormal—3 to 4 μg. per 100 cc. of serum
Possible hypothyroidism	Low normal—4 to 5 μg. per 100 cc. of serum
Euthyroidism	Normal—5 to 7 μg. per 100 cc. of serum
Possible hyperthyroidism	High normal—7 to 8 μg. per 100 cc. of serum
Hyperthyroidism	High—More than 8 μg. per 100 cc. of serum

tivity of the thyroid epithelium itself, there will not be any increase in either the uptake of radioactive iodine or in the value for the protein-bound iodine, whereas in cases in which hypothyroidism is due to failure of pituitary stimulation, with a responsive and productive thyroid epithelium, the uptake of radioactive iodine and the value for the protein-bound iodine will be greatly increased.[10]

It is apparent that the etiologic and quantitative classifications do not make use of a clinical syndrome. This results from the opinion that the symptomatic and somatic effects of varying degrees of hypothyroidism fail to produce any clear-cut clinical picture. Prolonged athyreosis of several years' duration, of the athyreotic type and of the most severe grade, does lead to the development of myxedema, which causes such a profound change in the appearance and function of the patient that the diagnosis often can be made at first glance or by merely hearing from afar the croaking, gutteral voice of the patient. But the young woman who has had several spontaneous miscarriages because of hypopituitary hypothyroidism in successive pregnancies has no symptomatic complaint that she can describe to her doctor or any alteration of physical appearance which he can observe, yet she is as seriously in need of thyroid therapy as the patient with gross myxedema.

Treatment

At present, all forms of hypothyroidism must be treated by substitution therapy. In the future, some means of improving pituitary function probably will be discovered that will allow the large number of patients with hypopituitary hypothyroidism to be treated by restorative functional therapy, and it may well be possible to promote the growth of thyroid tissue and restore the athyreotic hypothyroid patient to normal activity. At present, however, all types of hypothyroidism must be treated by the administration of substitution products. The best of these, in my opinion, is synthetic sodium levo-thyroxin.* As a result of improved methods of manufacture and recent chemical discoveries, the combination of amino acids with iodide has allowed the production of pure levo-thyroxin on an economical basis.[11] This material has been shown to be consistently potent in relieving hypothyroidism,[12] when given by mouth. Because of its reliable, permanent and exact hormone content, it is to be recommended as standard thyroid medication. The equivalent dose as compared with desiccated thyroid U.S.P. is 0.1 mg. to 1 gr. The individual requirement for maintenance may vary from 0.1 to 1 mg. administered by mouth daily. Overdosage to the point of thyrotoxicosis medicamentosa can occur, as is true of the older form of animal product.

Certain principles of substitution therapy in hypothyroidism may be emphasized. In the initial treatment of far-advanced, severe degenerative myxedema, the amount administered should be very low until primary tissue changes have occurred. A dose of 0.025 mg. of sodium levo-thyroxin may be administered orally once a day, for the first two weeks, following which 0.05 mg., and, later, 0.1 mg. may be administered daily with safety.

The serial observation of electrocardiograms is an extremely valuable guide to adequate thyroxin therapy. The T waves rise to normal as the tissue effects of thyroxin occur, and increase for several months to high voltages if the dose of thyroxin is excessive. Just as the proper diagnosis of hypothyroidism requires a determination of the circulating thyroxin (PBI), the control of substitution therapy should be accomplished by serial determinations of the protein-bound iodine at intervals of three months at most, until a steady state has been achieved. This may require a progressive increase of dosage to lead to an average protein-bound iodine value of 6 μg. per 100 cc. of serum, which may be accepted as the ideal normal level.

In many cases it will be found that during the earlier months of treatment a particular dose will be associated with a decreasing rather than an increasing concentration of protein-bound iodine as the higher levels of circulating hormone are required. This "fall-

*The sodium levo-thyroxin (TRAVENOL®) used in these studies has been provided generously by the Travenol Laboratories, Inc., of Morton Grove, Illinois and Los Angeles, California.

ing-away" phenomenon has been emphasized previously.[8] It may be imagined that the increasing metabolism of all the tissues, the greater rapidity of the circulation, and, doubtless, the increasing renal and hepatic metabolism of the administered hormone lead to the gradual reduction in circulating thyroxin, even though the oral dose has seemed adequate. For example, a daily dose of 0.2 mg. of sodium levo-thyroxin may have produced a concentration of 5 μg. of protein-bound iodine per 100 cc. of serum, which, after a few weeks with exactly the same dose, is found to be only 3 μg. per 100 cc., and a daily dose of 0.4, 0.6 or even 0.8 mg. may have to be administered, until a steady concentration of 6 μg. of circulating protein-bound iodine per 100 cc. of serum is accomplished.

The old dictum that the dose of desiccated thyroid was that which made the patient feel well is erroneous because the relief of symptoms begins with the early administration of small doses, and no upper limit of a sense of well-being is definable by the patient. I have regularly found that patients who state that they have benefited by the medication are still grossly undertreated when judged by biochemical measurements of the circulating thyroid hormone. A close analogy would be the treatment of secondary anemia by the administration of iron merely to the point at which the patients say they feel better, even though the value for the hemoglobin is decidedly below normal.

I, therefore, urge the oral administration of increasing doses of thyroxin until the dose that will continuously and indefinitely maintain a normal level of circulating protein-bound iodine is reached. In cases of hypopituitarism in which the concentration of protein-bound iodine is subnormal or moderately low before treatment, the daily dose may be considerably greater (0.2 mg.) than that used in cases of degenerative myxedema. The falling-away phenomenon is commonly observed in such cases, and a gradual increase in the dose over a period of time is required.

The treatment of hypothyroidism during pregnancy is important to prevent a miscarriage. The dose of thyroxin should be adequate to maintain the concentration of protein-bound iodine at least 50 per cent above the patient's normal level. The value of 9 μg. per 100 cc. of serum should be regarded as the lower limit of normal during pregnancy, and the dose necessary to attain this value should be administered. It is surprising that this dose may not be much increased. There is perhaps a transport protein mechanism involved, so that smaller doses achieve a higher level of circulating protein-bound hormone.

Most patients who have goiters have hypothyroidism. This would seem contrary to the thought that enlargement of the thyroid is indicative of increased thyroid function. In fact, such is rarely the case, and patients with so-called toxic goiters or toxic adenomas actually form a small minority of all goitrous patients. The occurrence of the goiter with postoperative compensatory hypertrophy or spontaneous hypertrophy is usually an indication that the body needs more thyroid hormone than it is receiving. It, therefore, is advisable to estimate the degree of hypothyroidism in patients with goiters. The administration of thyroxin may be expected to decrease the size of the goiter and to prevent the possibility of future hyperthyroidism.[13]

The demonstrated reduction of goiters by thyroid medication provides the concept for treating thyroid cancer that has been adopted by my colleagues and me.[14] It has been shown that malignant lesions of the thyroid in animals are associated with increased thyrotropic hormone.[15,16] In all cases of cancer of the thyroid observed at the Thyroid Clinic of the Los Angeles County Hospital, large doses of thyroxin are administered daily by the oral route after the initial treatment has been completed. The dose administered is adequate to maintain the concentration of protein-bound iodine at 6 μg. per 100 cc. of serum. This medication causes a depression of the thyrotropic pituitary hormone, which might promote the growth of the cancer of the thyroid and cause metastasis.

When the adequate maintenance dose of thyroxin has been established by prolonged observation, it is necessary to convince the hypothyroid patient that the need for the

medication will never cease. It is common experience to have even intelligent patients, who apparently understand their disorder, reduce the dose or discontinue the medication under the impression that their lack of a productive thyroid hormone mechanism has been cured.

The indefinite need for thyroid hormone is well illustrated by an extraordinary case which was reported to me through the courtesy of Dr. S. Gordon Ross. The patient, who is now 97 years old, has been taking thyroid since she became myxedematous at the age of 37 years. Her continuous need for this medication has been verified on several occasions, when the dose was deliberately reduced by her physician. It may well be imagined that some of the degenerative disorders of senility might be prevented by the continuous administration of thyroxin in the required amount.[17]

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MEETINGS *and Postgraduate Courses*

American College of Chest Physicians: Eighth annual postgraduate course on diseases of the chest at the Bellevue-Stratford Hotel, Philadelphia, March 7-11. Further information may be obtained from the Executive Director, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

College of Medical Evangelists School of Medicine, Los Angeles: Annual alumni postgraduate convention, February 15-17, 1955, at the Biltmore Hotel, preceded by two days of refresher courses at White Memorial Hospital. Further information may be obtained from Dr. Walter B. Crawford, 316 North Bailey Street, Los Angeles 33, California.

University of Minnesota, Minneapolis: Continuation course in neurology, February 7-12, at the Center for Continuation Study. Course will stress diagnosis and management of neurologic problems most frequently encountered. Guest speakers will include Dr. G. Milton Shy, Dr. Howard Fabing and Dr. Edward B. Schlesinger. The annual Johnston Lecture will be presented by Dr. Seymour S. Kety. Joint directors of the course will be Dr. A. B. Baker and Dr. William T. Peyton.

University of Minnesota, Minneapolis: Continuation course in recent advances in internal medicine for internists at the Center for Continuation Study, February 14-16, under the direction of Dr. C. J. Watson, Professor and Director, Department of Medicine.

University of Minnesota, Minneapolis and the Minnesota Division of the American Cancer Society: Continuation course in cancer detection for general physicians February 17-19, 1955, at the Center for Continuation Study.

University of Minnesota, Minneapolis: Continuation course in clinical hematology for physicians at the Center for Continuation Study, February 28-March 2.

Normal Eyes, Abnormal Eyes, and 20/20 Vision

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A COMMON misconception, particularly on the part of laymen, is that central visual acuity of 20/20 indicates entirely normal vision and that, conversely, any deviation from this measurement is evidence that the eyes are diseased or at least that glasses are necessary. We felt that it would be helpful to review the meaning of 20/20 vision and to study the common eye conditions in which this measurement yields useful information.

The designation 20/20 indicates that the individual was examined with the test chart 20 feet away and that he described a test symbol which subtended an angle of five minutes at that distance. It is important to know that 20/20 is not a fraction but only two numbers. Marked inaccuracies are introduced not by measuring at distances other than 20 feet, which is permissible, but by converting these findings to give the appearance of having tested at 20 feet.

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SHELDON ZINN

The ability to read the 20/20 line implies a fair degree of attention, moderate intelligence and good motivation in recognizing and describing test symbols of that particular size. The conditions under which vision should be measured have never been authoritatively defined. A wide variety of test charts, symbols, projections, mirrors and the like are used. Thus, an individual may have 20/20 vision with one set of test conditions and poor vision with another. This variation was particularly

evident in the Armed Forces, where a wide variety of tests was used with markedly different physical conditions and varying degrees of motivation to read or not to recognize the test letters. Since the war, the Subcommittee on Vision of the National Research Council has made encouraging progress toward standardizing this testing in the military services.

The 20 foot test distance was chosen as standard many years ago because at that distance all rays are practically parallel. The eye thus reacts to these rays as it does to rays emanating from infinity. Light rays from sources closer than this are divergent rather than parallel and introduce a factor of accommodation.

The five minute test symbol evolved from the idea entertained by nineteenth century astronomers that if two stars subtended an angle of less than one minute at the eye, they could not be distinguished separately. It was felt that a standard test symbol should be constructed so that each detail subtended one minute and the total symbol subtended five minutes. However, test letters vary considerably in legibility apart from their size. L is recognized much more readily than E, which is more distinct than B. On most test charts, easy and difficult letters appear on each line.

The finding of 20/20 vision indicates that the area of the visual axis is clear, i.e., that the lens and the cornea are clear centrally and there are no dense opacities preventing the image from impinging on a relatively normal foveal area. It also implies that the particular portion of the optic nerve and tract serving the foveal area is intact from the eye to the occipital lobe, and that the higher centers used in discrimination and form sense are normal. It does not, however, imply that the eyes are without disease and may not require correcting lenses.

In regard to the refractive error, 20/20 vision indicates quite definitely that myopia or simple near-sightedness is not present. It is entirely possible and indeed most likely that the patient has some degree of far-sightedness or hyperopia. The younger the individual the greater the degree of hyperopia that can be overcome without symptoms and with distinct vision. As accommodation decreases with increasing age, additional effort is required and the patient may have vague complaints known colloquially as "eye strain" and covering a large group of ocular conditions. Occasionally the effort of excessive accommodation to compensate for marked hyperopia and to maintain clear vision results in anomalies of the convergence mechanism so that an insufficiency occurs. These symptoms increase in severity with close work and are largely relieved when work of this type is omitted.

Visual acuity is no clue to the magnitude of refractive error. It is entirely possible for one individual to have 20/20 vision with a given refractive error while another can read only 20/40 with the same refractive error. When myopia is present, this may be due to individual adaptation in recognizing a blurred image. In other instances it is due to additional accommodation available to the one with the clearer vision.

Glaucoma

Glaucoma is commonly associated with entirely adequate and normal 20/20 vision. In simple glaucoma (or, in the old terminology, open-angle glaucoma) the field defect and the disease may be far advanced by the time central vision is affected. In narrow-angle glaucoma, central vision is again not involved except with the onset of an acute glaucomatous crisis. Usually the symptoms are so severe that medical attention is quickly sought and the disease is thus frequently recognized before ocular damage is marked. The testing of central visual acuity is almost entirely without value in surveying large groups of individuals for the presence or absence of glaucoma.

Cataract

The development of cataract, which is a generic term used to designate any loss of transparency of the crystalline lens, may or may not be associated with a decrease in central vision. As long as that portion of the lens directly in the visual line is unaffected, central vision may remain good. Indeed, occasionally one sees a patient with developing nuclear

sclerosis and consequent myopia whose vision without glasses improves as the lens becomes more dense. This "second sight of the aged" carries a disturbing prognosis, because ultimately the near-sightedness increases, and cataract extraction will be required if the patient lives long enough.

Other cataracts affecting primarily the visual line may be associated with relatively early loss of vision, although by and large the entire lens is almost transparent. However, if the axial area of the lens becomes opaque enough, cataract removal may be required, even though the peripheral lens is clear. These are the patients whose vision commonly improves, although never to the 20/20 level, with dilation of the pupils. Many of the old remedies for cataract consisted of some form of belladonna, which dilates the pupil widely. Such treatment, of course, is contraindicated because of the frequent coexistence of glaucoma in such eyes.

Other Visual Defects

Field defects arising from brain tumors and from interference with the optic tracts and radiation commonly are associated with normal central vision, although the defects may be marked. The papillomacular fibers, which carry central vision fibers, may remain uninvolved for a long period, and may not be involved at all, even though half of the visual field has disappeared as a result of pituitary tumor or other intracranial disease. Even when severe papilledema is present secondary to a large intracranial lesion, central vision is not infrequently 20/20.

An uncommon condition associated with normal central vision, but pointing up its relative unimportance when considered alone in the assay of visual function, is the optic atrophy seen in central nervous system syphilis. The peripheral field of vision may be reduced to an area of one or two degrees, although vision is 20/20. Such persons are economically blind and must be led around, because the small patch of acute vision is not adequate for any ordinary tasks.

Despite all these examples indicating that 20/20 vision is not necessarily an absolute indication of normal eyes, it must not be understood that there is no need for examination. Rather, it is important to realize that central visual acuity is only a portion of the measurement of visual function. As many a presbyope has learned to his dismay, 20/20 vision is not a guarantee that magnifying lenses for reading are not required as loss of accommodation becomes evident at 45 years of age. Many an individual with 20/20 vision and rather marked hyperopic astigmatism knows that the maintenance of clear vision causes so much discomfort that correcting lenses are preferable.

The eye with 20/20 vision may be described as normal only if, in addition to clear central vision, reading vision is adequate, with or without correcting lenses; color vision is normal; the peripheral field of vision is normal; there are no defects in that area of central vision within 30 degrees of the fixation point, and the two eyes can be used simultaneously and move normally. Lastly, if careful ophthalmoscopic examination of the disk indicates no abnormalities, the blood vessels are good, the macula is normal, and the peripheral fundus shows no disease, then it is justifiable after refraction to conclude that the 20/20 vision is associated with a normal pair of eyes.

Diseases of the macular area may be associated with 20/20 vision, although in such cases careful ophthalmoscopic examination foretells an ultimate loss of central vision. The central portion of the fovea, the so-called central bouquet of cones, contains about 25,000 cone units which are most important to central vision. As long as this central bouquet remains, the patient will be able to read 20/20 test symbols in spite of widespread macular disease. When the central bouquet of cones is lost, even though the remainder of the macular area is normal, central vision is markedly reduced. This explains the frequently paradoxical situation in which a patient with widespread macular disease still has normal vision, whereas another patient with perhaps only a couple of dots of senile macular degeneration has greatly reduced central vision.

There is considerable variation in the use of the terms fovea, macula, fovea centralis and the like to indicate the rod-free central area at

the posterior pole of the eye. Many physicians use them interchangeably and even consider them synonymous. These terms carry different connotations to the anatomist and to the ophthalmologist. To the anatomist, the macular area is that area permeated by a yellow pigment which diffuses through the inner layers of the retina and occurs only in primates. According to Polyak it is evident in the eye for only 15 minutes after death and can be recognized only after the eye has been opened. Its boundaries are the disk temporally, and about the same distance lateral to the central foveal reflex. It extends 4 or 5 mm. above and about the same distance below. It thus encompasses far more than the rodless area of the posterior pole and generally more than ophthalmologists mean by the macular area. However, since it is permeated with yellow pigment, it fulfills the semantic requirement of being the macula or yellow spot. The area with cones only is about 1 mm. in diameter. In the center of this area there is located a central bouquet of cones. These are long cones which anatomically resemble rods rather than cones, although physiologically they are entirely different. Because of their length, these cones bulge forward very slightly, producing a convexity which causes the central light reflex at the fovea seen ophthalmoscopically. Because of the thinness of this area, pigment shines through more clearly than elsewhere, and gives rise to the characteristic pigmented appearance. It is probably incorrect to apply the term fovea to anything but this 1 mm. area. The term fovea centralis should be used to designate the central bouquet of cones.

The full visual capacity of the eye is not present at birth. At about one year of age, 20/200 vision is normal, and at about two years the normal measurement is 20/40. Vision of 20/30 is about average at three years, and 20/20 develops about the fourth or fifth year. Sometimes this development is delayed until the seventh or eighth year, but at any time after this, vision of less than 20/20 is abnormal. Vision may be tested clinically at about the third year, using special charts. Surveys at this age are particularly useful because appropriate corrective measures may be taken if vision is defective. If surveys are postponed, as is usually done, until the sixth year or later, it is usually too late to correct any defect and to prevent amblyopia ex anopsia.

Measurement of central vision is particularly important following minor eye injuries. Many persons have never tested their vision monocularly and discover for the first time, after a cinder has been removed, that vision is defective in that eye. If vision was not measured prior to treatment, this abnormality may be wrongfully attributed to the treatment rather than to the pre-existing defect.

Many persons with less than 20/20 vision see normally when looking monocularly through a small pinhole in a card. This simple test usually indicates that the visual defect is due to a refractive error rather than organic disease.

POSTGRADUATE CONTINUATION COURSE
University of Colorado School of Medicine

Psoriasis, Seborrheic Dermatitis and Pityriasis Rosea

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PSORIASIS

PSORIASIS is a chronic or recurrent scaly eruption of unknown origin whose frequency, tendency to recur and resistance to treatment make it one of the most common dermatologic problems. It affects both sexes in approximately the same proportion and begins most commonly between the ages of 15 and 30 years, although the initial attack may occur at any age. Psoriasis is primarily a disease of white people and is seen very infrequently in Negroes.

The disease usually begins with bright red, sharply circumscribed spots which soon become covered with adherent, dry, micaceous scales. Lesions vary from pinhead-size to large patches covering extensive areas of body surface. They generally are solid patches, but instead of the plaques one may see large or small, complete or incomplete, gyrate, circinate lesions with partially to completely cleared centers. The eruption may be limited to a single lesion or may extend over most of the body surface. Removal of the scales often leaves a moist surface with numerous tiny bleeding points. This is considered by some as a diagnostic point for psoriasis, but it may be seen in other situations.

Psoriasis universalis may develop as an erythematous exfoliative dermatitis or may be converted into such by improper or irritative treatment. Subjective symptoms are usually absent in the chronic form of psoriasis, but there is usually some degree of itching in the acute form, or that stage of the disease during which the eruption is spreading rapidly. Psoriatic lesions in the genital, perianal and intergluteal regions are generally pruritic. There is usually a seasonal variation, with spontaneous improvement in the summer months, and spread and development of new lesions in the winter. Trauma may influence psoriasis, as evidenced by the patches which develop at points of abrasion or excoriation or in surgical scars.

Arthritis is associated with psoriasis in a small proportion of cases, approximately 2 to 3 per cent, and generally takes the form of a polyarthritis affecting the small joints of the

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hands and feet. This type of psoriasis occurs two or three times more commonly in women than in men.

The course of psoriasis is variable, with frequent or occasional recurrences or remissions in the same case. One attack may be widespread and severe, whereas another may be limited and mild in extent. One attack may respond quite readily to treatment; another may be highly resistant—also in the same case. Lesions in some areas may persist for decades without improvement and without further extension. In general, it may be said that the course of psoriasis is chronic and that the disease is difficult to manage. Some patients simply learn to live with the disease, while others, even with mild forms, suffer great mental anguish.

The most common sites of psoriatic lesions are the scalp, the nails and the extensor aspects of the extremities, particularly the knees and elbows.

Seborrheic psoriasis of scalp.

Scalp

Psoriasis of the scalp is characterized by flat or elevated, fairly discrete, erythematous, scaly or crusted plaques of varying size. These may be palpable through the hair and are seen most commonly around the scalp margins; frequently they extend beyond the hairline to the forehead or postauricular region. In another form the scalp is covered diffusely with dry, gray-white scales on a mildly erythematous base. In contrast with seborrhea or seborrheic dermatitis, psoriasis of the scalp is generally not associated with alopecia.

Nails

Psoriasis of the nails takes various forms. There may be simple stippling, with little groups of pits in the nail plate. The nail plates may be quite thin, dull, friable and longitudinally ridged, and in this form, too, there may be stippling. Another change is the presence of one or more yellowish-brown, waxy-appearing spots beneath the nail plate. Finally, the most characteristic nail change in psoriasis consists of yellowish-brown wedges at the lateral margins of the nail plate. This portion of the nail usually separates from the nail bed, and yellowish, crumbly epithelial debris accumulates under the detached nail.

Palms and Soles

Psoriasis may involve all the palms and soles or just one, or more. One sees sharply localized, small, scaly papules or large, diffuse, slightly scaly, erythematous areas. Lesions may be pink, red or yellowish-brown and vary from fine scaling to markedly hypertrophic, hyperkeratotic thickening with deep fissuring.

Psoriasis of the palms and soles.

Other Sites

Other common sites of psoriasis are the sacral area and the glans penis; in a case of the latter, the disease must be distinguished

Psoriasis of the trunk, diffuse.

Psoriasis under breasts.

from lichen planus, drug eruption, and a precancerous condition known as erythroplasia of Queyrat.

In contrast to the usual extensor involvement, there is a form of the disease which is called psoriasis inversa and which involves the flexors, particularly the axillae and the inguinocrural, perianal and periumbilical regions. Such lesions are usually bright red and macerated, and lack the scaly character of the usual eruption.

Cause

In spite of extensive research, the cause of psoriasis remains unknown. There is an irregularly dominant hereditary tendency to development of psoriasis in about 30 per cent of the cases. Repeated attempts have been made to link psoriasis with some faulty metabolism of proteins, carbohydrate or lipids, particularly the latter. However, these studies are inconclusive. During World War I, when there was a scarcity of food in Germany, particularly a shortage of fats, the incidence of psoriasis decreased materially there. Possible roles have been ascribed to various microorganisms found in scale scrapings or stained tissue. Arguments against the infectious origin are equally convincing, however, and one may conclude that this hypothesis has no more firm foundation than the endocrine or metabolic theories.

Treatment

As is the case in any disease process for which the cause is unknown, the treatment of psoriasis is varied and may or may not be successful. I have selected just a few prescriptions, the ones which I feel have withstood the test of time.

Mercurial and tar preparations—These two agents are commonly used interchangeably, i.e., after a few months' treatment with tar, its effectiveness fades and mercurial preparations are used. Ammoniated mercury is an old standby and is used in 2 to 6 per cent concentration. Mercurial reactions are likely with greater concentrations. As shown in the prescription below, the preparation contains salicylic acid, which is almost always incorporated in a salve for psoriasis in order to obtain some degree of exfoliation, softening and removing of the top layer of scales—to get down to the base of the lesion.

Mercurial

Ammoniated mercury	0.6-1.8
Salicylic acid	0.6-1.8
Anhydrous lanolin	12.0
Petrolatum q.s.	30.0

Sig.: Rub into affected parts three times a day.

Any one of the types of tar listed below may be used, again with salicylic acid and in a greasy ointment base, because one of the

Tar

Crude coal tar	2-10%
Birch tar (oleum rusci)	3-10%
Juniper tar (oleum cadini)	3-10%
Solution coal tar (LCD)	5-20%

ONE OF THE ABOVE IN:

Salicylic acid	0.6-1.8
Petrolatum q.s.	30.0

Sig.: Rub into affected parts three times a day.

essentials in topical therapy of psoriasis is the vigorous application of the medication into the psoriatic patches. An old trick is to take a soft toothbrush with which to rub it in, or to wrap a piece of cloth around the head of an old-fashioned clothespin and dip it into the jar of ointment and massage that vigorously into the lesions.

Chrysarobin—Chrysarobin is a very good therapeutic agent in psoriasis; however, it must be used with considerably more care in selection than either the mercurial or the tar preparations. It stains badly, and accidental contamination of the eye produces rather severe conjunctivitis.

Chrysarobin

Chrysarobin	3.0
Salicylic acid	3.0
Petrolatum q.s.	60.0

Sig.: Massage into skin twice daily.

ANTHRALIN® ointment 0.1-1.0%

Sig.: Massage into skin twice daily.

Goeckerman treatment—This is a combination treatment including ultraviolet (either the machine or natural sunlight) and some tar ointment. The old-fashioned way is to massage the ointment vigorously into the skin the night before exposing the entire body to ultraviolet rays. Care should be exercised so that no more than a mild transient erythema is produced. A useful modification is the application of solution of coal tar immediately before exposure to ultraviolet light.

X-ray therapy must be judiciously used in any chronic, recurrent skin disease, because the total dose can get away from you and radiodermatitis can result.

Psoriasis of the scalp—The same remedies are applicable in treatment of psoriasis of the scalp as in treatment of lesions elsewhere on the body, with the exception of chrysarobin which may stain hair or cause conjunctivitis. Also, one has to be perhaps a little more vigorous in terms of rubbing the ointment into the affected skin of the scalp than in treatment of lesions on glabrous skin, in order to get it down to the base of the lesion. The ointment base used should be water-soluble to facilitate washing and to avoid matting of the hair. A stimulating, cleansing scalp lotion for daytime use in a case in which the psoriatic patches are thin, with not too much scaling or piling up, is the following:

Resorcinol mono-acetate	4.0
Salicylic acid	2.0
Bichloride of mercury	0.2
Glycerin	4.0
Alcohol 70% q.s.	240.0

Sig.: Apply to scalp each morning.

Any preparation that seems to cause irritation and/or spread of the lesions should be discontinued and another tried.

Systemic therapy—Two old standbys in the heavy metals department are arsenic and bismuth. Fowler's solution has definite value, but one must bear in mind that untoward effects follow the prolonged use of arsenic. Good therapeutic control is necessary with its use. Try to keep it limited to your own administration rather than letting the patient use it ad libitum.

Bismuth is definitely helpful, in the form of injections or oral tablets (BISTRIMATE®).

Diet—Many patients who are on the chubby side or definitely overweight relate that their psoriasis improves spontaneously when they diet carefully and lose weight.

ACTH or cortisone—Use of these two steroids should be very limited in cases of psoriasis. Severe arthropathic psoriasis and the generalized erythrodermic type are really the only two good indications for their administration.

Vitamins—Improvement often follows the administration of vitamin A and/or vitamin D in large doses, 100,000 units a day. Lesions recur, however, following discontinuance of such therapy.

Psychotherapy—I did not mention psychic influence as a cause of psoriasis, yet one sees a pronounced variation among patients in terms of their acceptance of or their rebellion against the condition. A generous portion of psychotherapy frequently helps immeasurably in the management of cases in which the usual means fail to relieve the condition.

SEBORRHEIC DERMATITIS

Seborrheic eczema or dermatitis may be defined as a subacute or chronic inflammatory

disease affecting the seborrheic areas or areas most richly supplied with sebaceous glands. I will not consider simple seborrhea, which is a state of oiliness, waxiness or dry scaling in the seborrheic areas, and which responds to the same but milder measures and is regarded as the background for the development of seborrheic eczema or seborrheic dermatitis.

The sites of predilection in seborrheic eczema are the scalp, face, ears, presternal and interscapular regions, the periumbilical and pubic regions and the axillae. The clinical picture varies from case to case, but in general it may be divided into two types: (1) scaly, erythematous type that occurs in the usual seborrheic areas and (2) the moist, fissured type which involves the flexures.

The usual onset of seborrheic dermatitis is the appearance of one or more small erythematous spots covered with greasy or yellow scales. The lesions gradually increase in size to form well-defined nummular or polycyclic patches with central yellow-tinted zones and erythematous papular margins. Central clearing may occur.

Scalp

On the scalp, seborrheic dermatitis is generally diffuse, or it may consist of erythematous spots covered with yellowish, greasy or, on occasion, fine branny scales. The patient complains of moderate to severe itching, general discomfort and occasionally some degree of hair loss. Lesions may become crusted, oozing and elevated, in which case they may simulate psoriasis. In milder forms of seborrheic dermatitis of the scalp there may be diffuse, yellow, waxy or greasy scaling on a mildly inflamed base.

Involvement of the scalp is commonly accompanied by scaling and erythema of the ears, usually at the external auditory meatus or in the postauricular area. Retroaural lesions often become secondarily infected, with acute inflammation, oozing, crusting and fissuring which may extend down the side of the neck. Scalp lesions may also extend forward to the forehead. The glabellar area, eyebrows and nasolabial folds are commonly involved.

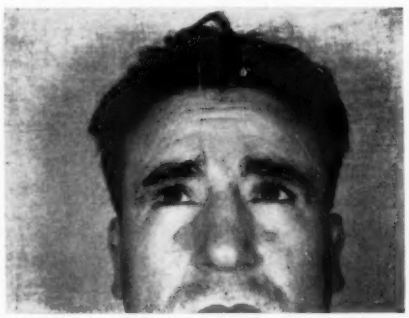
Papular Type

The papular variety of seborrheic dermatitis usually affects the forehead and sides of the face but may develop on the trunk, arms and thighs. The individual lesion in the papular type is a small, lentil-sized to pea-sized, slightly scaly or moist, exudative, crusted, deep-red papule.

Flexural Type

The flexural type of seborrheic dermatitis presents a remarkably different picture. Regions usually affected are the axillae, the postauricular and inguinocrural areas, the intergluteal cleft, the pubic area and the umbilical area. The eruption starts with small, erythematous, scaly or moist, exudative spots and spreads to form large plaquelike lesions. If untreated, the eruption will spread and usually becomes moist, oozing, and bright orange-red

Seborrheic dermatitis simulating lupus erythematosus (before treatment).



Seborrheic dermatitis, axilla.

in color, with crusting at the margins and scattered satellite lesions around the adjacent surfaces. The degree of local discomfort depends on the degree and extent of the eruption, but it is generally pronounced.

The intergluteal fold is a common site of seborrheic eczema and may be the only area involved, in which case one will be hard pressed to distinguish it from psoriasis or intertrigo or tinea. Seborrheic eczema of the axillae involves the vault of the armpit in contrast to contact dermatitis, which usually affects the margins and spares the apex.

Blepharitis

Blepharitis is a common aspect of seborrheic eczema affecting other areas and is often seen in cases of moderate to severe involvement of the scalp, eyebrows and glabella. The extent and severity of the lid margin dermatitis varies from mild erythema to edematous, crusted, itching and, at times, lichenified varieties.

The course of seborrheic eczema is usually chronic, with frequent flares and remissions. It generally is seen in postadolescents and adults but may occur in infancy, in which case it must be distinguished from infantile eczema. Some authorities consider seborrheic dermatitis and psoriasis variants of the same disease. In borderline cases, differentiation is difficult or even impossible clinically or even histologically.

Cause

Two schools of thought exist concerning whether the bottle bacillus, a yeastlike fungus, or *Pityrosporum ovale*, is responsible for seborrheic dermatitis. Some groups have incriminated this fungus as the causative agent, but the majority consider it a saprophyte.

Constitutional background is an important factor. Aberrant or excessive secretion of sebum and abnormal keratinization permit excessive growth of bacteria and fungi which are said to predispose to seborrheic dermatitis.

Endocrine factors must be considered in any discussion of the cause of seborrheic eczema. The onset of symptoms at or shortly before puberty suggests an endocrine influence. The acne and familial alopecia which often are seen in combination with seborrheic dermatitis are associated with endocrine disturbance, particularly of the sex glands. It may be assumed that seborrhea generally bears some relationship not only to the sex glands but perhaps also to the pituitary, thyroid and adrenal glands and to disturbances in the hypothalamic centers or the midbrain. Seborrhea is common in cases of epilepsy, brain injury or mental deficiency, and some association with these conditions is probable.

Many authorities consider dietary factors important in the etiology of seborrheic dermatitis. Some drugs; foods such as chocolate and shellfish; condiments; excessive quantities of oils, greases and fried foods; bromides and iodides sometimes appear to act as accessory exciting influences.

Environmental factors have been credited with causing seborrheic dermatitis. Poorly ventilated or overheated rooms or apartments are said to favor development of seborrheic eczema.

Treatment

Treatment of seborrheic eczema resembles closely that of psoriasis. However, by and large, topical medications for seborrheic dermatitis rely more on a sulfur-resorcinol combination than on mercury and tar, although the latter do have a definite place in therapy.

SCALP OINTMENTS

Sulfur (Ppt.)	3.0
Salicylic acid	1.8
Resorcinol mono-acetate	1.8
AQUAPHOR® q.s.	60.0

Sig.: Massage into scalp three to seven nights a week.

Ammoniated mercury	1.8
Salicylic acid	1.8
Neo-Base q.s.	60.0

Sig.: Massage into scalp three to seven nights a week.

SCALP LOTIONS

Resorcinol mono-acetate	4.0
Salicylic acid	2.0-4.0
Bichloride of mercury	0.2
Glycerin	4.0
Alcohol 70% q.s.	240.0

Sig.: Massage into scalp three to seven nights a week.

Bichloride of mercury	0.1-0.2
Chloral hydrate	4.8-9.6
Spts. formic acid 1%	15.0
Castor oil	2.4-7.2
Alcohol 90% q.s.	240.0

Sig.: Massage into scalp three to seven nights a week.

GLABROUS SKIN

Sulfur (Ppt.)	1.8
Aquaphor or Neo-Base q.s.	60.0

Sig.: Massage into skin twice daily.
(Note: Efficacy may be enhanced by adding salicylic acid, resorcinol, etc.)

PRAGMATAR®

Sig.: Massage into skin twice daily.

The scalp lotions are useful in those stages where the heavy crusting, the thick lesions, have been thinned down by previous applications of salves. I want to mention particularly SELSUN® Suspension, a selenium sulfide preparation, which has a definite place in the treatment of seborrheic dermatitis of the scalp. I think its use should be limited to milder cases or to those in which only the thin, dry, scaling patches remain. It may be used as a shampoo or as a rinse following a shampoo, and in this regard I might mention that the patient should avoid detergent shampoos and use ordinary soaps. Selsun breaks down when mixed with some detergents.

Treatment of seborrheic eczema in the flexural areas is by and large that of any acute, exudative, oozing disease in that part. One must dry up the lesions and reduce the inflammation before applying any of the antiseborrheic remedies. Wet packs, mild pastes and lotions are used. Once the acute edema and erythema have subsided, small quantities of sulfur or resorcinol may be added.

FLEXURAL AREAS

Wet compresses: Boric acid or Burow's solution.

Paste:

Burow's solution	10.0
Anhydrous lanolin	20.0
Lassar's paste q.s.	60.0

Sig.: Apply three times a day.

Lotion:

Burow's solution	30.0
Zinc oxide	
Talcum, purified	
Glycerin	
Lime water AA q.s.	240.0

Sig.: Apply three times a day.

BLEPHARITIS

Yellow oxide of mercury, ophthalmic, 2%
Antibiotic ointments, ophthalmic
Hydrocortisone ointment, ophthalmic

Systemic therapy—Here again there is much duplication with the treatment of psoriasis, with more emphasis on vitamin B complex, liver, vitamin B_{12} and riboflavin. In severe cases medicated baths may be helpful. ACTH and cortisone may be indicated in widespread, incapacitating cases, but use of these agents should be limited.

PITYRIASIS ROSEA

Pityriasis rosea is a skin disease of limited duration, characterized by an erythematous, scaly eruption. It is more common in the spring and autumn seasons. The age incidence is highest between 15 and 40 years. Moderate pruritus may accompany the early phase of the eruption, although many patients have no local symptoms whatever. Mild constitutional symptoms may precede the appearance of the eruption, which lasts for from 3 to 10 weeks and then begins to clear spontaneously. One episode usually gives lasting immunity.

In most cases, an initial or herald patch precedes the generalized eruption by a few days to two or three weeks. This lesion is erythematous, scaly, occasionally circinate, and measures from 2 to 5 cm. in diameter. Its size increases slowly and it is commonly mistaken for a ringworm infection and treated as such. New lesions appear and spread rapidly for a few days to about two weeks. They are pale red, oval and dry, with a fawn-colored or yellowish central portion and a finely crinkled surface which is referred to as cigaret-paper wrinkling. A collarette of white scales often surrounds the periphery. The lesions in pityriasis rosea measure from one to several centimeters in diameter. Typically there is fairly diffuse involvement of the trunk and extremities, with lesions predominating on the chest and proximal portions of the arms and thighs and a tendency to concentration about the inguinal and axillary areas.

On the trunk the long axes of the oval patches tend to run parallel to the normal lines of cleavage. Rarely do lesions appear on the face, scalp, palms and soles, or mucous

membranes. Vesicular lesions are sometimes seen but are confined to the palms and soles. A mild generalized adenopathy may accompany the skin rash. As the individual lesions of pityriasis rosea slowly increase in size, they become tan to brown in color and then finally begin to fade. Scarring or pigmentation rarely results.

Cause

Most evidence points to an infectious origin of pityriasis rosea, although the exact cause is obscure. Exposure to new clothes or to the elements, nervous shock, drugs and diet appear to be related to the onset of symptoms, but are regarded usually as precipitating factors rather than direct causes.

Treatment

Ultraviolet therapy may be given every few days to produce mild desquamation. Starch baths may be of help. Reduction in the amount of soap used, together with applications of mild lotions or emulsions, will make the patient more comfortable. Antihistaminic agents and sedatives are administered as needed.

Postgraduate Clinical NOTES

30. BACKACHE AND THE DISC

In the terminology of Hollywood it is now some twenty years since Mixter and Barr "discovered" the intervertebral disc. Since that time its popularity has grown, at first slowly but with gathering impetus, until it is now probably at the pinnacle of its fame and therefore qualifies to be included in the limited group of subjects considered suitable material for music-hall jokes. Psychologists, of course, have long pointed a warning finger at the hidden significance of jokes, but all that an orthopaedic surgeon can deduce probably from this phenomenon is that the term "the disc" has now reached a stage of universal misunderstanding. . . .

Another aspect [of treatment] is the relation of a patient's temperament to his disease. In these days of rush anxiety many patients are temperamentally unable to accept the limitations of treatment, particularly when the treatment may involve a change in their way of life which is prolonged or permanent. In effect the proposition that they put to their doctor is that they wish to be cured, but in no circumstances will they undertake any treatment inconvenient to themselves. They are in consequence attracted by the reputation of any practitioner, orthodox or unorthodox, who will promise a quick, if not instantaneous, cure, and it is only if the doctor has a definite and rational plan of treatment worked out that he can avoid the pressure to undertake a series of often empirical treatments in no very definite order in the hope of achieving some spectacular result. On the other hand, the doctor must realise that the disease is not fatal, and therefore he must at all times take care not to institute treatment which is worse than the present state of the disease. This necessitates an accurate assessment of the disability caused by the condition initially, the patient's normal way of life and responsibilities, experience with the methods of treatment used, and an attention to detail in those methods.

G. K. Rose, *The Lancet*, June 5, 1954, p. 1143

BOOK CHAPTER*

Medicine 1954

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OUTSTANDING among steps in medical progress in 1954 were perfection of the vaccine for infantile paralysis with the mass experiment to determine its value; introduction of several new drugs including chlorpromazine, DIAMOX®, Rauwolfia, and lysergic acid; surgery of the heart; and improvements in the use of the x-ray for diagnosis. The vaccine against poliomyelitis which was the featured development of 1953 was improved and the largest mass experiment in the history of medicine is now under way to determine its efficacy. Many new antibiotics have been announced and are undergoing experimentation. New hormones, biologic preparations, and diagnostic technics were published.

Chlorpromazine hydrochloride,[1] known also as THORAZINE® and LARGACTIL®, exerts unique effects on the nervous, blood vessel and muscular systems of the body. It produces sedation without hypnosis, relaxation of muscles and lowers greatly the temperature of the body. Numerous investigations indicate potential uses in almost every branch of medicine. Chlorpromazine has been particularly effective in controlling the anxiety and agitation that occur in manic-depressive psychosis, schizophrenia and psychoneurosis. Results have been dramatic in treatment of nausea and vomiting due to various causes. The drug enhances the action of many pain-inhibiting and anesthetic drugs.[2] Among other conditions treated have been the pain and vomiting of terminal cancer, and even hiccoughs. Another use has been the prevention of the usual adverse reaction between alcohol and the anti-alcoholic agent known as ANTABUSE®.

Rauwolfia serpentina is a plant of the dogbane family which is gathered in the foothills of the Himalayas. The drug, which is prepared from the plant's roots, has been used in India for thousands of years. The product lowers the blood pressure and slows the pulse rate. Because of its safety it is used with other more powerful drugs to control hypertension. Several alkaloids have been found in

*This article is condensed from a chapter of the book "Medical Progress, 1955," edited by Morris Fishbein, M.D., to be published by the Blakiston Division, McGraw-Hill, Inc., New York.

the root and are being studied as to specific effects.

Diamox is a potent carbonic anhydrase inhibitor which acts as a diuretic by causing loss of bicarbonate ion through the kidney, thus eliminating sodium, potassium and water and retaining ammonium.[3] The drug is being used especially in congestive heart failure and in emphysema. Because of its special properties the drug is tried in cases of epilepsy, disturbed renal function and some gastric conditions. Five tissues of the body are known to be stimulating to carbonic anhydrase activity—the kidneys, lining of the stomach, pancreas, brain and red blood cells. Some of the effects related to these tissues are still obscure.

D-lysergic acid diethylamide has been used in research on psychiatric patients. The drug is related chemically to ergot. It induces psychic states in which repressed memories and other material in the unconscious mind are brought to light. Soon after its use emotional activity is stimulated. With this is a sense of lightness and withdrawal from reality. Drs. Sandison, Spencer and Whitelaw[4] of Powick Mental Hospital near Worcester, England, have provided a clear description of the patient under the influence of lysergic acid.

The authors consider that lysergic acid primarily disturbs the unconscious, and that subsequent phenomena depend on the result of the action of the unconscious or consciousness, so that they are bound to vary from patient to patient. The authors are convinced that the drug, used as an adjunct to skilled psychotherapy, is of great value in the treatment of obsessional and anxiety conditions accompanied by mental tension. The knowledge gained may lead to a better understanding of schizophrenia.

Medicine advances in epochs such as the periods of bacteriology, vitamins and hormones. Now comes the era of the enzymes. Already used widely in medicine are trypsin, which dissolves pus, dead tissue and heavy mucus from the lungs; hyaluronidase, which loosens connective gluelike material that binds cells and thus softens scar tissue and aids absorption of injected drugs; streptokinase and streptodornase, which also aid the breaking up of secretions and drainage of infected matter from the body. VARIDASE® (streptokinase-streptodornase), a preparation widely used in surgery for the dissolution of blood clots and pus by local application, can also be administered intramuscularly to bring about a reversal of the process of inflammation.

Although the exact mode of action of streptokinase is not known at present, the agent probably begins a series of changes ending in the dissolution of fibrin. The body responds to injury or infection by attempting to localize an abnormal condition, forming a mechanical barrier composed of fibrin clots in the tissue spaces surrounding the affected area. While performing a useful function, the fibrin barrier at the same time keeps out red and white blood cells and antibiotics of sulfonamides which control infection. Streptokinase removes the barrier so that circulation to and from the area is improved.

Antibiotics

Research on antibiotics continues to yield new products and improvements on old ones.

The greatest gains have been made against the beta hemolytic *Streptococcus*, *Pneumococcus*, *Gonococcus*, *Meningococcus*, *Bacillus anthracis*, *Pasteurella tularensis*, *Past. pestis*, *Hemophilus influenzae*, *H. pertussis* and *Shigella*. According to Dr. Harry F. Dowling, these infections respond promptly to proper doses of antibiotics, and resistant strains apparently do not appear in patients. Dr. Dowling reported nearly as good results with antibiotics in a second group to which organisms causing syphilis and brucellosis belong.

Antibiotics have so far made little headway against viruses except those which cause parrot fever, trachoma and lymphogranuloma. AUREOMYCIN® chlortetracycline has produced excellent results in the treatment of brucellosis or undulant fever due to *Brucella abortus*, the commonest form of the disease. The effectiveness of the various antibiotics and other drugs on the disease has been extensively studied since 1937 at the University of Minnesota Brucellosis Research Center.

Superior results have been obtained by administering dihydrostreptomycin and a tetra-

cycline drug such as Aureomycin or TERRAMYCIN® simultaneously. Some investigators have added sulfadiazine to the streptomycin-tetracycline combination with favorable results.

Another promising development in brucellosis treatment is the use of hydrocortisone with the dihydrostreptomycin-tetracycline. The hormonal therapy is recommended only for seriously ill patients.

Puromycin, not yet commercially available, is reported effective against amebiasis experimentally induced in guinea pigs. Puromycin also slows the growth of one kind of breast cancer transplanted into mice. Another product derived from impure cultures of penicillin has a similar effect.

Psittacosis, or parrot fever, which has worried public health officials because of the popularity of parakeets as pets, can be eliminated if the breeders have the birds treated with Aureomycin chlortetracycline or Achromycin tetracycline—Aureomycin. K. F. Meyer and B. Eddie of the George Williams Hooper Foundation, University of California, San Francisco, reported regular use of the product to cure human beings who contracted the disease from birds.

Mycostatin is the first broadly effective antifungal antibiotic. It is derived from cultures of *Streptomyces noursei.* Mycostatin inhibits or kills all species of fungi and yeasts tested, except *Actinomyces.* Against *Candida albicans (Monilia)* 1 unit or less per milliliter is effective. Its greatest effect is on yeastlike fungi in the growing state; it is less active against spores and is inactive against bacteria. Mycostatin is recommended for the prevention and treatment of intestinal moniliasis which develops during treatment with antibiotics.

Vitamins

Pyridoxine,[5, 5a] better known as vitamin B_6, was formerly said to be of little significance in relationship to human diet. Now it has been established that such symptoms as seborrheic dermatitis, inflammation of the tongue, and in some instances confusion and even loss of appetite may be related to a deficiency of this vitamin in the diet. Some of the symptoms of excessive oiliness of the skin with inflammation have been relieved by use of an ointment containing this vitamin. Deficiency of this vitamin has been related to a sensory neuritis developing in infants; also to convulsive seizures which occurred on pyridoxine-deficient diets. Reports have been published of uncontrolled absorption of iron without utilization after such deficiency. Other studies have indicated a possible role of vitamin B_6 in the function of the pituitary-adrenal gland system.

In a study of "Chronic disease and vitamin C," Drs. Leo J. Cass, Willem S. Frederik and J. D. Cohen[6] found that elderly persons show a low level of vitamin C in their blood, due possibly to a low vitamin C content in the foods they consume or to losses occurring in food preparation. Upon receiving orange juice or ascorbic acid they showed a rapid rise in the vitamin C level.

Fifty-three people with acne were treated with the ordinary treatment including, however, addition of large doses of vitamin C and citrus juices. Forty-three improved in four months and of these, 15 had previously been treated without any definite improvement. The improvement after the vitamin C and citrus juices was dramatic. They were given 8 oz. of citrus juice twice daily and 3 gm. of ascorbic acid each day. The British Medical Research Council found that vitamin C and citrus juices have an important part in certain cases of acne.

Rheumatic Fever

In prevention of rheumatic fever, present technics involve treating any sore throat at the earliest possible moment with antibiotic drugs. In one series a 200,000 unit tablet of BICILLIN® was given once each day to each patient. Some took the medicine before breakfast, others before lunch and others at dinner without any fixed time. As a result of this method, the children of school age lost only 193 days because of illness, while in the year before the same children lost 983 days. The bacteriologic studies showed that the streptococci disappeared from the throats and that there was no recurrence of rheumatic fever after the preventive technic was begun.

A substance called streptococcal proteinase has been isolated in crystalline form from the streptococci that are associated with attacks of rheumatic fever. Injected into experimental animals this substance causes damage to the muscles and valves of the heart, accompanied by inflammatory reaction. With only a few exceptions the destructive action caused by this enzyme was confined to the heart. Conceivably this is a direct approach to determining the cause of rheumatic fever which has not yet been established. The research may also provide the answer to the way in which infections of the throat by streptococci damage the heart.

A five year study on the use of penicillin taken by mouth to prevent recurrences of rheumatic fever was completed in the Department of Cardiovascular Research of Michael Reese Hospital, Chicago.[7] Eight hundred thousand units of penicillin were given by mouth daily for seven days of each month of the school year. Cultures for the typing of the special *Streptococcus* that has been associated with acute rheumatic fever were taken from the noses and throats of the children. About 150 children were studied. One group received penicillin while the other did not receive such preventive drugs. The average number of recurrences each year in those who did not receive drugs was 22 compared to 0.66 in those given penicillin. Thus it was proved that penicillin is effective in lowering significantly the recurrence rate of rheumatic fever for three successive years.

Dental Caries

Investigators have been trying to identify a specific cause for the premature decay of the teeth that is called caries. The majority of evidence now indicates that the best method of preventing caries is the use of a well-balanced diet. However, contributing factors may be the use of carbohydrate foods and such delicacies as sticky candies and taffies which adhere to the teeth and form a culture medium for the bacteria that attack dental tissues. Apparently it is the sticky carbohydrates that are chiefly at fault rather than various drinks and foods containing sugars. Fluoridation seems to be established as helpful in prevention of caries. Many municipalities are adopting fluoridation of water supplies toward this end. However, referendums held in several large cities in the elections in November 1954 resulted in defeat of these proposals.

Coronary Thrombosis

"Manager's disease" is a name given to the heart and blood vessel disorders that are prevalent among and cause death prematurely to executives, lawyers, foremen, physicians and important administrators. Angina pectoris and coronary thrombosis are included. The mortality of men in such positions from the age of 45 to 60 is 45 per cent above that of the over-all male population. Studies[8] made at the Institute for Industrial Hygiene in Germany credit this high mortality to "working fever," failure to take adequate week-end recreation and holidays, lack of proper relaxation and insufficient sleep.

Most people who survive a blocking of the coronary artery—coronary thrombosis—live for many years and are able to lead a productive life. Physicians studied 400 patients who had survived an attack for 3 to 28 years. Thirteen per cent had lived more than 10 years and an additional 26 per cent over five years. Almost half of them made a recovery sufficient to allow them to continue normal living. The best guide as to likelihood of complete recovery was the symptoms—not the age of the patients, or the electrocardiogram or the roentgen-ray pictures.

Surgical Procedures

Surgery has developed more procedures for operating on the heart, including the famous "blue baby" operation, opening constricted valves that result from rheumatic disease, and providing new circulation for cases of coronary thrombosis. Cooling has been found successful in slowing the circulation and is accomplished by the use of iced baths or ice packs, chlorpromazine, intravenous use of HYDERGINE® with PHENERGAN® and pethidine. The drugs lower the body temperature below 87 degrees. Clamping of the large blood vessels is done to produce a bloodless heart. This

was achieved without ventricular fibrillation, the heart flutter which almost inevitably is fatal. Above the 87 degree temperature this development was avoided by injecting a local anesthetic into the sinus node, the pacemaker of the heart.

All the cardiovascular changes in animals transformed to hibernation with either the Hydergine or Thorazine combinations were reversible during the rewarming period. This method of artificial hibernation, according to Dr. Jean Cahn[9] of Paris, makes it possible to interrupt coronary circulation or to arrest the whole circulation up to 25 minutes and to perform ventriculotomies. The drug combinations used in the experiments block the autonomic functions at different levels and protect the organism against stress reactions due to the lack of oxygen.

Another surgical procedure involved a substitution of a child's blood circulation during an operation on the heart by connecting it to one of the child's parents or to a donor of the same type of blood and restoring the circulation after the operation.

An amazing surgical procedure has been devised for children with hydrocephalus.[10] The operation has been performed on 50 infants, mostly between three and six months of age. The investigator reports 31 who had satisfactory results. Seventeen infants have died and 33 in all are still living. The operation consists of removal of one kidney, usually the left, and the placing of a polyethylene tube into the ureter, the duct that carries the urine from the kidney to the bladder. The other end of the tube is put in the spinal column in the lower portion. In all, 30 patients have been followed for more than two years. Of the 33 still alive, only one is retarded mentally to the point of needing institutional care. Five others are slightly behind the normal developmental schedule but are making progress. Of the remaining children, 24 are said to be in excellent health with normal or close to normal mental and motor developments. The cause of death in those who failed to survive was usually meningitis.

Operations to relieve backache and other pains due to pinching or slipping of the cartilaginous disk between the vertebrae were much studied during 1954. Improved methods of diagnosis called attention to the great frequency of this condition.[11] When the soft cartilaginous disks between the small bones of the spine in the region of the neck slip out or get pinched, the symptoms are serious and persistent, including pain and stiffness and difficulty of motion. Treatment includes the application of heat to the muscles at the back of the neck, massage with deep stroking, kneading and stretching, pulling with a traction of 40 to 60 pounds twice a day. Among 61 patients with this condition seen in a large clinic, only 20 per cent required surgical treatment. A number of devices have been invented for putting the necessary pull or stretching on the neck. One of these is called a "tractolator." It provides rhythmic, intermittent traction with the patient in a sitting position for from 15 to 30 minutes. The largest amount of traction that can be applied by this device amounts to 35 or 40 pounds.

An embolus[12] blocks the flow of blood through the blood vessel. With lack of blood, the tissues die. Formerly many arms and legs were removed because of embolism. Now embolectomy has been improved. In one clinic nine successes were obtained from 15 such operations in 13 different patients over a four year period. No patient died as a result of the operation and no limbs were lost in the last seven cases. The operation should not be denied to patients because they are old or have hardening of the arteries, because success has been obtained in four patients 71 to 80 years of age.

Whiplash injury[13] of the neck is the name given to a sprain of the neck in which there is injury to the nerve roots from stretching or compression or a direct blow. The injury follows a sudden and forceful bending of the neck. Usually the person is sitting in a normal position in an automobile and a collision from behind thrusts the body forward with an acute, sudden bending of the neck. Generally there follows immediately a bending backward and stretching. Sixty-two per cent of 50 cases had a momentary lapse of consciousness at the time of the injury with a blinding

or explosive sensation in the head at the time of the crash. The complication that was most distressing was a persistent psychoneurotic reaction which handicapped the person in his work. Injury of the lower back was a complication in 15 out of 50 patients. Most of the patients are given rest in bed for 24 to 72 hours, usually in a firm bed, and treatment with drugs to overcome the pain and restlessness. When the neck symptoms are intense, a collar is worn to prevent further jarring of the neck such as occurs when riding in a car, walking over rough ground and similar conditions. Warmth is applied but not extreme heat. Warm baths help to overcome the tension. As a preventive, it is urged that drivers keep those behind informed of stops and turns by the use of proper hand signals and stay at safe stopping distance behind the car ahead.

Skin Disturbances

Great progress is under way in conditions affecting the skin. In the pituitary gland a hormone has been found related to deposit of pigment in the skin. It is called the melanocyte stimulating hormone.

Eczema in infants is definitely related to sensitization to various substances. In the New York University Post-Graduate Medical School[14] and in Bellevue Medical Center, cortisone ointment was used on 30 cases and was compared with a similar ointment without cortisone used on the opposite side of the body. Favorable response to the treatment was noted in 18 patients. The investigators are convinced that in the general run of cases, the application of cortisone ointment is the simplest, cleanest and most rapidly effective of all the measures that have been employed by application to the inflammation in the treatment of infantile eczema.

Cortisone ointment has also been used with great benefit in the treatment of itching of the anus, between the buttocks, and in genital itching in women.

Investigations have been made on underarm odor[15] as to the role of bacteria, presence of sweat and use of deodorants. Twenty healthy men were studied. The sweat in the axilla is odorless and sterile when it appears. The germs present under the arms act on the sweat and promote the development of the typical acrid odor within a few hours. Control of these germs will prevent any odor. Without the sweat there would be no odor. The extensive use of hexachlorophene-detergent preparations will abolish the odor for more than 18 hours in most people. The presence of hair under the arm increases the odor since it acts as a collecting place for the secretions, the debris, the peeled skin and the germs. Simply shaving and washing of the armpit will eliminate the odor for more than 24 hours. Ordinary sweat, whether sterile or unsterile, does not have an odor and does not develop odor but through accentuation of bacterial growth can produce an odor. The investigators found that the aluminum preparations have some detergent activity and that daily application of these substances will diminish or abolish the odor in many persons for 12 to 18 hours. This effect is due to their antibacterial action and their chemical effect on the sweat. The aluminum salts did not have any effect in reducing the amount of sweat.

Pigmentation of the skin or lack of it disturbs people far beyond its seriousness as an illness. A product for use in vitiligo (white spots on the skin) will probably be released for general sale by the Food and Drug Administration in the near future. The drug is a derivative of an Egyptian plant called Ammi majus Linn. Extended studies by some 100 dermatologists indicate that this is the first medical treatment for the condition to have actual effect. The drug is taken by mouth and two hours later the skin is exposed to ultraviolet rays. Over a long period of time the skin becomes pigmented in the white areas.[16]

In contrast is another new discovery for cases of unnecessary pigmentation such as occurs in chloasma or "liver spots." This product, known as monobenzyl ether of hydroquinone (BENOQUIN®), removes pigment from the skin by blocking the body's action in forming pigment. A 5 per cent ointment applied once weekly caused depigmentation of chloasma after eight months. Some persons with excessive vitiligo instead of trying to pigment the white areas have used the treatment to

remove pigment from the adjacent areas, particularly on the face.[17,18]

New X-Ray Technic

A new ultrasonic photographing device combining the principles of sonar, radar and television gives well-defined pictures of the body's internal soft organs and tissues. This device, called the "Somascope," is said to reveal goiters, cysts and tumors. The person is placed in a tub of water where ultra-high frequency sound waves are produced. Electrical energy is converted by a quartz or barium titanate ultrasonic crystal into sound waves which pass through the water and are reflected back from the surface of the body, picked up and converted into electrical signals which are amplified and passed into a cathode ray tube which shows them as bright spots on a TV screen. This makes a two-dimensional picture which can be photographed for permanent record.

Demand Feeding

One hundred years ago babies were fed from the breast or the bottle whenever they cried.[19] Fifty years ago the four-hour feeding interval became the rule and worked well except that some mothers observed the time interval too rigidly. Now demand feeding is being boomed again with the idea of giving the baby what it wants when it wants it. However, many specialists in the care of babies are resisting the revival of demand feeding, claiming that the baby is fed too much and too often but that the stress is worse on the mother who actually prefers the moderate regular schedule and is able to lead her own life and care for the rest of the family. Thus she can regulate her life, her work and her scant leisure. A compromise has been suggested that the baby regulate the night and the mother the day feedings.

Physical Therapy

Spasticity with tightness and tension of muscles and ligaments is a painful condition and is often treated by orthopedic surgeons by stretching. Recent observations show that greater relaxation follows electrical stimulation of spastic muscles. The old argument as to whether to apply heat or cold has been settled since the investigators found that the immersion of the limb in cold water at 50° F. for five minutes aided relaxation of spasm more than the application of heat.

Improved Sunglasses

An ophthalmologist[20] reports that the selection of pink for colored glasses and of aquamarine for windshields is unfortunate since it interferes with vision in night driving. He emphasizes that modern windshields were made green because large areas of glass let in too much heat from the sun. The green filter cuts out the red and infrared rays which carry heat. However, the green is a bad selection from the point of view of permitting vision during night driving. Tests showed that the ability to see is greatly decreased by the use of such tinted glass. The tests indicated that normal vision which is 20/20 decreases to 20/34 through light yellow glass, 20/40 through pink glass and 20/46 through the green windshield. The worst combination is the combination of pink glasses and a green windshield which decreases visual ability to 20/60.

Poliomyelitis

The Third International Poliomyelitis Conference was held in Rome in September 1954. The subjects chiefly discussed were the use of a preventive vaccine and the social aspects of medical care and rehabilitation. Much attention and research have been devoted to respirators for bulbar paralysis. A safe vaccine has been developed and is being produced on a large scale at a reasonable cost. In the experimental stage, it has certainly proved capable of raising the level of protective "antibodies" in the blood. No doubt a short series of injections of vaccine will safely and permanently protect against poliomyelitis. The mass experiment involving inoculation of more than half a million children and an equal number of controls will be reported in April 1955. In the meantime, research is continuing on the use of a living, attenuated virus as a vaccine. For development of tissue cultures of poliomyelitis virus which made

possible preparation of a vaccine, Enders, Weller and Robbins received the 1954 Nobel prize.

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BOOKS RECEIVED

New books received are acknowledged each month. As space permits, books of principal interest to our readers will be reviewed more extensively. Reviews will be found in this issue starting on page A-118.

Growth and Development of Children. By Ernest H. Watson, M.D., Professor, Department of Pediatrics and Communicable Diseases, and George H. Lowrey, M.D., Assistant Professor, Department of Pediatrics and Communicable Diseases, University of Michigan Medical School, Ann Arbor. Ed. 2. 296 pages. 1954, The Year Book Publishers, Inc., Chicago. $7.00.

The Management of Endocrine Disorders of Menstruation and Fertility. By Georgeanna Seegar Jones, M.D., Assistant Professor of Gynecology, The Johns Hopkins University, Baltimore. 198 pages, illustrated. 1954, Charles C Thomas, Springfield, Illinois. $5.75.

Atlas of Congenital Cardiac Disease. By Maude E. Abbott, M.D., Curator of the Historical Medical Museum and Assistant Professor of Medical Research, McGill University, Montreal, Canada. 62 pages. American Heart Association, Inc., New York. $5.00.

Progress in Clinical Surgery. Edited by Rodney Smith, M.S., F.R.C.S., Surgeon, St. George's Hospital, London, England. 414 pages, illustrated. 1954, Little, Brown & Company, Boston. $6.50.

The Bane of Drug Addiction. By Orin R. Yost, M.D., Fellow of the American Psychiatric Association. 155 pages. 1954, The Macmillan Company, New York. $4.00.

Stellate Ganglion Block. By Daniel C. Moore, M.D., Director, Department of Anesthesiology, Mason Clinic, Seattle. 280 pages with 101 illustrations. 1954, Charles C Thomas, Springfield, Illinois. $10.50.

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MENTALLY RETARDED CHILDREN

AMONG the 31,000,000 children now attending school, there are about 700,000 who are mentally retarded to the degree that they need some special assistance. All of these children have been seen repeatedly by physicians. In far too many instances, however, the physician, being unable to do anything medically for the child, has left the family to fend for itself in trying to plan for the child's future.

In some instances of extreme mental retardation, such as mongolism, cretinism, microcephaly and hydrocephaly, there are sufficient physical signs either at or shortly after birth to make the diagnosis obvious. In most instances, however, there are no physical signs of retardation, and diagnosis of its degree, cause and the prognosis of future potentials is a highly technical matter requiring the coordinated efforts of the pediatrician, neurologist, psychiatrist, psychologist, educator and frequently, other medical specialists.

When there are no obvious physical signs, but when the physician suspects mental retardation, he should confirm this suspicion by observing the physical and social growth of the child before reporting such suspicion to the parents. Is unusual placidity or extreme fretfulness evident in the first six months? Does he attempt to sit up? To grasp? To play? To demand attention? To follow simple directions? Does he do these at a slower rate than within the range of normal expectations?

If, based on these and other signs of physical and social behavior, the child at the age of three appears retarded as much as a year, his condition is likely to prove permanent unless it is caused by ill health or unsatisfactory environment. By the time the child is four, there should be little doubt in the physician's mind. Sometime during this period, as his suspicions become confirmed, he should take the parents into his confidence and explain carefully and humanely the nature of the child's problem and what can be expected. His responsibility does not end here, however, for he should assist the parents to sources of help in planning for the child's future and also in adjusting to their own emotional reactions to the condition. Unfortunately, far too many parents discover that their children are men-

tally retarded only when the child, entering kindergarten or the first grade, is unable to cope with this experience.

The parents should be brought to understand that:

1. The condition is not curable. The child will not "outgrow" it.

2. Though the child cannot become normal, parents can do much for his welfare.

3. Social service agencies, special school programs, and other groups in many communities stand ready to help.

4. Habit and character training is possible for even the most severely mentally retarded children.

5. Parents should not prevent their child from doing as much as possible for himself. He should not be overprotected.

6. Possibilities of delinquent and antisocial behavior among such children are real.

7. The welfare of the other children in the family should not be jeopardized by the retarded child.

One very simple thing the physician can do which will be of immeasurable assistance to the parents is to put them in contact with the local organization of the National Association for Retarded Children, 129 East 52nd Street, New York 22, New York. Founded in 1950, when a number of local groups of parents of retarded children banded themselves together, this organization now has 325 locally affiliated chapters in 46 states with a rapidly growing membership exceeding 40,000 families. Although a relatively new organization, it has already been extremely influential in increasing facilities of all kinds for such children and in serving as a national clearing house for information on mental retardation. In addition to the extremely valuable, practical information which parents may receive from this group, the knowledge that hundreds of thousands of other parents have been faced with the same problem and have successfully coped with it is of great emotional value to them.

Of the various booklets on mental retardation which a physician might keep handy in his office to give to parents the day he must first confront them with the word that their child will "never grow up" is the excellent Public Affairs Pamphlet, "New Hope for the Retarded Child," by Walter Jacob. Single copies are available for 25 cents from Public Affairs Pamphlets, 22 East 38th Street, New York 16, New York.

No one can say accurately how many mentally retarded children there are in the United States, for "mental retardation" is a relative term. Authorities estimate, however, that one in every thousand is retarded to the point that he is "dependent" and will need full-time care throughout his life.

Four in every thousand are listed as "semidependent." This means that although they can be trained to the point of self-care and social acceptability, they probably will never be able to earn a livelihood.

Twenty-five in every thousand will never acquire a mental age of over 12 even in adulthood. With special services, however, they can be trained to get along independently, with limited judgment and ability.

Several studies are being made to gather more definite information on the prevalence and degree of mental retardation. There is no doubt, however, that the problem is sizable, affecting not only an estimated 3 per cent of our total population but the victims' families and communities as well.

In contrast to previously accepted concepts that most mental retardation is inherited, more recent studies have shown that more than half of all cases come from causes in which heredity is not a factor.

Children of mentally normal or superior parents are frequently affected as a result of damage to the nervous system during the fetal period or at birth. The condition may also result from an infection of the brain tissue (encephalitis) or of the tissue covering the brain (meningitis).

Until recent years the approach to the problem was to place the dependent and semidependent groups in institutions, and to ignore the larger number of children who could achieve limited independence with special services. Whenever possible children were placed in either state or private institutions, where they received an educational program

consisting of normal matter brought down to their mental level.

The cost of providing good care and specialized instruction for such children is necessarily high, and many parents are unable to place their children in the approximately 200 private home-schools for such children in the nation. The factors of whether a home-school is state or privately operated is not the important issue.

There are some excellent state-operated schools, just as there are some excellent private schools. Since state schools usually handle larger numbers of children, the private school may offer more individual attention and a better chance for both educational and social achievement.

The fact that children in state schools sleep in dormitories, eat in centralized facilities and participate in more group activities, however, is not of itself undesirable. There is always, of course, the danger that such large institutions may lose the highly desirable "home atmosphere."

Whether the school be a public or private institution, the primary factor in its quality will be its personnel, for they determine its atmosphere and competency.

Some advancements are now being made in developing educational programs outside of institutions for such children. Some states provide "home instruction" for preschool children and their parents, and some communities have established special classes, nursery schools, day schools, vocational training programs, guidance services and other special activities.

Among the most promising of these new developments are the 500 public and 250 parent-sponsored, private day classes now in operation throughout the country for children in the semidependent group who previously have been excluded from public schools. These special classes not only reduce the cost of the care and training of such children but also permit them to be taken care of by their families in their own communities.

With proper training, either at home or in a specialized institution, many mentally retarded persons can learn to work successfully. This was particularly evident during the war when the manpower shortage permitted many, for the first time, to find jobs. Properly placed in jobs that do not demand normal mental ability, and given adequate supervision, they frequently make superior employees, particularly in the many tasks which are so simple, repetitive or monotonous that they are dissatisfying to the person of average intelligence.

The greatest handicap that the nation's 700,000 mentally retarded children face is not their low mental ages but the public's lack of understanding. Mental retardation stands today about where tuberculosis did 50 years ago, venereal disease 30 years ago, and mental illness as little as a decade ago. It is the physician's responsibility to aid society in finding out what these children can do and then to give them the chance to do it.

HOWARD A. RUSK

THE INTRODUCTION OF VITAMIN D IN NUTRITION

THE history of medicine is replete with instances of discoveries made accidentally or by the process of serendipity; other investigations have led to successful results by well-conceived hypotheses and the development of accurate protocols for controlled experiments. The story of vitamin D represents a combination of both processes.

The term *vitamin* came into medicine about 1911. Dr. Genevieve Stearns,[1] research professor of pediatrics at the State University of Iowa, has recently published a retrospect of her early experiences with vitamin D in the nutrition of infants and children. About 1920 she came to the State University of Iowa to work on infant nutrition with Dr. Amy L. Daniels. At that time Dr. A. H. Byfield was head of the department of pediatrics and was undertaking many interesting studies. In 1922 came the report that cod liver oil contained two vitamins, the second of which was known as vitamin D, the rickets-preventing factor. Looking back at this time, Dr. Stearns recalls that Dr. Byfield was certain that the efficacy of cod liver oil was in direct proportion to its

unpalatability. Dr. Daniels had stumbled onto the value of cod liver oil because babies eating partly skimmed milk grew so well and thrived so amazingly when a small amount of cod liver oil was added to their formulas.

In 1924 Dr. Philip Jeans came to the University of Iowa. He observed the studies that had been made under Dr. Byfield and Dr. Daniels. In that same year Head and Steinbach had observed independently that foods, like children, could develop vitamin D when given ultraviolet irradiation. Dr. Stearns points out that soon everything from milk to sausage was being irradiated to provide the marvelous new vitamin. About that time these matters came before the Council on Foods of the American Medical Association which became involved in curbing the injudicious addition of vitamin D to a variety of foods. I well remember the early Council discussions when most of the membership agreed that it would be desirable to irradiate infant foods which were lacking in this factor, but that under no circumstances should milk, bread or any of the staples of life be modified by adding this essential vitamin.

The years have passed and today the Council on Foods agrees with other councils and commissions that children have greatly benefited by the ultimate decision to add vitamin D to milk. Dr. Stearns suggests that the dictum of the Council on Foods that vendors of 400 unit vitamin D milk could make greater advertising claims than those selling 1.35 unit vitamin D milk sounded the knell of irradiated milk. Odd flavors developed when milk was irradiated to high potency. The expense of the equipment and the relaxation of laws in individual states which permitted adding vitamin D concentrates to milk brought about the change. Today all vitamin D milk recognized as such contains 400 international units per quart. Similarly the decision of the Evaporated Milk Association to add 400 units of vitamin D per reconstituted quart of milk to all evaporated milk without an increase in price has proved an important public health measure.

The early years of the study of vitamin D were marked by many controversies and arguments which required carefully conducted experiments, particularly such as those made by Jeans and his colleagues, to permit final decisions. Today milk fortified with vitamin D is available almost everywhere in this country and nearly all evaporated milk is fortified.

Bread is today the only other food recognized by authoritative bodies as suitable for fortification with vitamin D, but as yet relatively little bread is so fortified. Presumably this addition is hardly necessary in view of the fact that growing children require little extra vitamin D beyond that usually received in their diets.

MORRIS FISHBEIN

1. Stearns, Genevieve: Early experiences with vitamin D in the nutrition of infants and children: A retrospect. Nutrition Rev. 12:193 (July) 1954.

WOMEN LIVE LONGER

The life expectancy of women is now much longer than that of men. Dr. Wilson T. Sowder[1] says that life expectancy of a white girl at birth in Florida is 73.9 years but a white boy at birth may expect to live only 66.7 years. The difference of 7.2 years has vast social, economic and political significance. In 1662 Captain John Graunt reported for London that more men than women are born and that more men die before their time. He also said, "Physicians say that they have two women patients to one man." The preponderance of women and the gradual control of more and more assets by women has given great concern to many observers of economic trends.

One of the factors related to these observations is the increase of lung cancer among men as contrasted with that among women. In 1950 the death rates per 100,000 from respiratory cancer were 24.1 for men and 5.4 for women, whereas in 1930 the rates were 4.8 for men and 2.1 for women. The rise has been credited to smoking, but there is not yet any evidence that the smoking by women, which around 1916 began to equal that by men, brought about a comparable rise in mortality rates for women.

In 1950 the death rates in the United States

for nearly all of the major causes of death were substantially higher among men than among women. The mortality rate among women was significantly higher only for diabetes, cancer of the breast and cancer of the genital organs. Death rates from suicide and homicide were three times as great among men as among women; accidental deaths were more than twice as frequent. Moreover, the tuberculosis death rate was more than twice as high among men as among women and the rates were also higher for poliomyelitis and pneumonia.

Various speculations have been offered to explain the increase in mortality rate for the male. The man is still the main breadwinner of the family and is, therefore, exposed to greater worries and pressures of modern life as well as to physical dangers. Women have, however, increasingly become employed and in many instances carry burdens greater than those of men. In England and Wales the mortality rate for men, particularly in the lower socio-economic levels, is related to their environment rather than to their occupations. Dr. Sowder suggests that the difference in reactions of men and women to modern life, including work, is more pertinent than the work itself. Women continue to escape the consequences of worry, frustration, disappointment and tension to a greater degree than men do by resorting more to tears, hysterical reactions and the ability to talk at great length about what disturbs them. Men, he suggests, react by developing coronary disease, hypertension or ulcers. The suggestion has also been made that women are better and more frequent customers of modern medical science than are men. They stay away from work for mild illnesses more than do men; they go to bed sooner and stay there longer when ill, and they are likely to follow the physician's instructions more faithfully. Moreover, social workers and social thinkers have been concerned far more with protection of women than with protection of men.

In his interesting study, Dr. Sowder offers the belief that men suffer from the ancient delusion that they are the stronger and superior sex, whereas the evidence indicates only that their muscles are stronger. In an earlier day big biceps had much more importance in the battle for survival than they do now. Today mental and emotional reactions are more significant than physical strength. The concluding suggestion seems to be that more attention can be given profitably to the health of men, and particularly to the health of middle-aged and older men. The statistics indicate that today the health hazards to men are the greater problem.

MORRIS FISHBEIN

1. Sowder, Wilson T.: Why is the sex difference in mortality increasing? Pub. Health Rep. *69*:860 (September) 1954.

ON BEING A WITNESS

In a fascinating essay, "Effective testimony for scientific witnesses," Dr. Wilmer Souder,[1] for 39 years a member of the scientific staff of the National Bureau of Standards, offers some valuable suggestions to those who, like physicians, find themselves not infrequently in court, on the witness stand, and subject to interrogation as to their competence, knowledge or reliability as observers. The first problem is the presentation of observations, knowledge or evidence in language understandable by the listeners. "Technical expressions, unless clearly explained," says Souder, "have no place in testimony before the average jury."

The medical witness particularly will find that many questions concern his qualifications. American attorneys are aware of differences between physicians and cultists, among medical schools, internships, residencies, membership in medical organizations, certification by boards, and similar qualifications. Since a mere diploma may be all that qualifies an expert, the opposing attorneys may spend much time going into the experience of the witness. There is the classic story of the general practitioner who qualified as an expert, and was asked questions in the field of pathology, and who then testified that he had never done a postmortem examination, whereas the expert called by the other side had done 20,000 necropsies.

Souder warns particularly against the phrase "I think." The expert is supposed to know or

to conclude that certain observations prove the statements that he makes. A witness has the right to admit that he does not know, that he cannot give a categorical answer to certain questions, or that he can answer only with reservations.

Here are a few aphorisms plucked from Souder's valuable experience:

> The expert should maintain the poise and dignity of a professional man. . . .
>
> Every real expert will admit the limitations to his abilities and the fact that there are borderline cases.
>
> If you do not speak loud enough for each juror to hear and understand every word, you are not a top expert.
>
> Take time to think over all questions. If you snap back answers to the attorney before he completes the question and slow up on cross-examination it will be noticed by the jury and may be interpreted as "in trouble."
>
> Some attorneys specialize in involved questions and hope for a single answer that may be correct for the last part of the question but not for the first or middle part.
>
> Be careful about giving unqualified endorsements for any textbook, magazine, writer, or official. Do not claim to know every line written on any subject.

Medical writings are replete with accounts of trials in which physicians have fallen victim to the astute or shrewd questioning of experienced lawyers. Similarly, many great medical witnesses have performed so notably as to have their replies recorded in medical history. Some 30 or 40 years have passed since the "expert medical witness," often trained as both physician and lawyer, was prominent in the American courts. Today any physician, general practitioner or specialist, may be called to testify as an expert. Unfortunately, few of our medical colleges have courses related to medicolegal testimony; some do not have even one lecture on the subject. In a concluding paragraph, Dr. Souder submits a competent analysis of the situation of the expert:

> The honest expert never looks upon the outcome of his work as a result of luck, the reward of a game, or victory in a battle of wits. He has built his qualifications through hard work. He establishes his conclusions through exacting procedures; he presents his testimony in the face of keen opposition and asks no favor beyond an honest consideration of the facts disclosed. Having done so he has fulfilled the high obligations of his profession.

In the light of my own rather considerable experience as a witness may I offer a few personal suggestions:

> Answer the question briefly and succinctly; do not lecture to the jury.
>
> When your attorney objects to a question of the opposition, wait calmly and silently until the controversialists get the matter settled by the judge.
>
> If you cannot answer a question and know where you can find the right answer, you may offer to look further for it.
>
> When the opposing counsel begins to tell you how good you are, *beware.*
>
> Do not quarrel with the attorneys—particularly your own—and certainly never with the judge.
>
> Stay away from percentages or mathematical ratios in conclusions unless prepared then and there to document them absolutely.
>
> Above all, speak simply and clearly!

To a pathologist an attorney said: "Please tell the jury as simply and clearly as possible the cause of death in the case here concerned." The pathologist answered: "The cause of death was cerebral hemorrhage, induced by essential hypertension, which in turn may have been related to chronic interstitial nephritis, chronic cholecystitis, or perhaps may have been psychosomatic in its etiology." A juror exclaimed: "Well, I'll be —— ————!" The judge remarked: "Perhaps I ought to reprimand you for that outburst, but the fact is, I was thinking exactly the same thing!"

The pathologist might have said: "He had apoplexy or a stroke, with high blood pressure, perhaps related to inflammation of the kidneys or gallbladder, or perhaps to some mental or emotional strain."

MORRIS FISHBEIN

1. Souder, Wilmer: Effective testimony for scientific witnesses. Science 119:819 (June 11) 1954.